Medical Tribune

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and Medical News

Vol. 17, No. 26 — *world news of medicine and its practice—fast, accurate, complete* — Wednesday, August 18, 1976

Flu Shot 'Risk-Benefit' Consent Form Planned by CDC

IMPORTANT INFORMATION ABOUT SWINE AND VICTORIA INFLUENZA (FLU) VACCINE (BIVALENT) — July 16, 1976

Special Precautions

As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, the flu vaccine has rarely been associated with severe or fatal reactions. In some instances people receiving vaccine have had allergic reactions. You should note very carefully the following precautions:

- Children under a certain age should not routinely receive flu vaccine. Please ask about age limitations if this information is not attached.
- People with known allergy to eggs should receive the vaccine only under special medical supervision.
- People with fever should delay getting vaccinated until the fever is gone.
- People who have received another type of vaccine in the past 14 days should consult a physician before taking the flu vaccine.

If you have any questions about flu or flu vaccine, please ask.

REGISTRATION FORM

I have read the above statement about swine and Victoria flu, the vaccine, and the special precautions. I have had an opportunity to ask questions, including questions regarding vaccination recommendations for persons under age 25, and understand the benefits and risks of flu vaccination. I request that it be given to me or to the persons named below of whom I am the parent or guardian.

INFORMATION ON PERSON TO RECEIVE VACCINE

Name (Please Print) _____ Birthdate _____ Age _____

Address _____ County of Residence _____

_____

_____

_____ Date

Signature of person to receive, or parent or guardian

FOR CLINIC USE

Clinic Ident. _____

Date Vaccinated _____

Manufacturer and Lic No. _____

The Center for Disease Control's swine flu vaccine "risk-benefit" statement (section of preliminary draft above) will have to be read and signed by all persons receiving the vaccine in a public health setting. In an interview with Dr. Arthur M. Sackler in this issue, Dr. Theodore Cooper, Assistant Secretary for Health, HEW, discusses the vaccine's field tests, possible toxicity, and pending indemnity legislation. See story below.

Rapid, 'Highly Accurate'

Simple Device Gauges Status Of Fetal Lung

By Nathan Horwitz
Medical Tribune Staff

New York—A simple, rapid and "highly accurate" device for determining fetal lung maturity in utero has been developed by an Israeli team.

Based on the use of fluorescent light to label lipid concentrations in a small sample of amniotic fluid, the device yields a printout of fetal lung status within one hour, and makes it possible to determine the optimum time for inducing labor in high risk pregnancies, the investigators said.

Dr. David M. Serr, Chief of Obstetrics-Gynecology, Sheba Medical Center, Tel Aviv, reported here that a study of 98 amniotic samples in 62 pregnancies showed the procedure gave "consistently reliable" results when checked against more conventional methods.

"There was no single case of respiratory distress syndrome in these complicated pregnancies, and all infants were discharged in healthy condition," he declared. Patients in the series included women with diabetes and severe hypertension.

The device, invented by Meir Shinitzky, Ph.D., a membrane research physiologist in the Weizmann Institute of Science, requires withdrawal of about one half milliliter of amniotic fluid by amniocentesis, and the addition of a fluorescent reagent to the sample to produce polarization labelling of the lipids under helium light.

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Dr. Cooper Discusses

Swine Flu Vaccine: Testing, Toxicity, Liability Problems

Medical Tribune Report

Dr. Cooper

Washington—"Vaccines and the use of vaccines have always been the subject of debate in this country and elsewhere," Dr. Theodore Cooper, Assistant Secretary for Health, Department of Health, Education and Welfare, said in an exclusive interview with Dr. Arthur M. Sackler, International Publisher of Medical Tribune. In the interview, Dr. Cooper discussed the acute toxicity data available, the degree to which the government should be liable in the event that persons sustain damage from the vaccine and the possible side effects.

Dr. Cooper said in the interview that

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Interview Text, P. 25

Stanford's 100th Heart Transplant Sparks Questions about Future

Stanford University Medical Center's heart transplantation team recently implanted a new heart in their 100th patient. Accordingly, Medical Tribune asked Dr. Edward B. Stinson, shown above at right operating with Dr. Norman Shumway, to comment on the team's future expectations. See interview on p. 20.

Multiple Sclerosis Advance

New MS Tests Abet Diagnosis, Drug Monitoring

By Anastasia Toufexis
Medical Tribune Staff

New York—Two new tests—one that could diagnose multiple sclerosis even in its early stages and another that could be useful in monitoring therapy of the disease—have been developed by independent teams of researchers from Duke University and Johns Hopkins.

The diagnostic assay, based on rosette formation of lymphocytes around measles-infected human epithelial cells,

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INTERNATIONAL REPORT

from Japan *from the Editors of Medical Tribune Japan, Tokyo*

New Hog Valve Bioprosthesis Implanted in 40 Heart Patients

Medical Tribune World Service

GIFU—The 40th meeting of the Japan Circulation Association here was told by Dr. Tsuguhito Tanaka, surgeon of the National Osaka Hospital, of the follow-up results over three years in 40 patients who were implanted with a bioprosthesis, a new type of artificial valve in which a hog's aortic valve is used as a part.

Mechanical valves and tissue valves are currently available, Dr. Tanaka said. However, mechanical ones have been found unsatisfactory in terms of hemodynamics, while the tissue type is handmade and offers very little in the way of uniform quality.

DR. TANAKA

On the other hand, the hog valve bioprosthesis, according to the researcher, seems to offer all-round qualities to meet the needs.

The meeting was also told by Dr. Yoshimasa Senoo, a surgeon at Okayama University, of the results from a cardiac morphological study conducted

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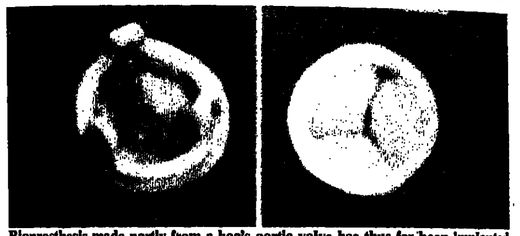

Bioprosthesis made partly from a hog's aortic valve has thus far been implanted in 40 patients at the National Osaka Hospital. New valve is said to offer advantages over both the mechanical and the tissue-type valves.

from Germany *from the Editors of Medical Tribune Germany, Wiesbaden*

Austrian Smokers Found at High Risk of Bladder Cancer

Medical Tribune World Service

VIENNA—Smokers are substantially more liable than nonsmokers to urinary bladder papilloma and carcinoma; the same applies also to former smokers, according to Dr. H. Flamm, of the Austrian Federal Institute of Public Health. Dr. Flamm recommends that as a prophylactic measure for early detection, increased attention ought henceforth to be paid to smokers as a group specifically exposed to risk.

Such considerably higher vulnerability of smokers present and past was disclosed by a large-scale, retrospective, epidemiologic study of bladder tumor patients as compared with a representative cross-section of the total population of Austria. The research was carried out by the Austrian Federal Institute of Public Health at the behest of the government. In Austria, 56% of the men are current or former smokers, whereas the proportion of smokers among bladder tumor carriers is 88%; of female patients, 37% were current or former smokers, while the proportion of women smokers in the population as a whole is only 15%.

The study covered 1798 patients from the years 1972-75. At the time of

Continued on page 28

from Britain *from the Editors of Medical News-Tribune, London*

'Vacuum Cleaner' Removes 100% of OR's Waste Gases

Medical Tribune World Service

LONLON—A draft of the directive from the Department of Health and Social Services asking hospitals to install systems to scavenge waste gases from operating theatres because of risks to staff is being circulated to the relevant bodies for consultation.

The warning comes after a nine-month inquiry carried out by the Association of Anesthetists into the dangers of working in operating theatres.

The circular also states that hospitals will not be given additional money to carry out the safety measures.

At a time like this, the choice of the winning film for first Harold E. Lewis Award for Research Films in the Brit-

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Effectiveness of "vacuum cleaner" system for removing anesthetic gases from different types of expiratory valves was demonstrated in prize-winning 16 mm movie. Emulsified vegetable oil and CO_2 were used to visualize gas flow.

from France *from the Editors of La Tribune Médicale, Paris*

Clinicians Explore Working Definition of Chronic Bronchitis

Medical Tribune World Service

CLERMONT-FERRAND—The problem of defining chronic bronchitis was discussed here by physicians at a round-table sponsored by *La Tribune Médicale*. The participants, in their daily practice, diagnose and treat chronic bronchitis patients. Brief highlights of the discussion follow:

Prof. Claude Molina, professor at a pulmonary clinic and hospital, internist, led off the discussion by giving his definition of chronic bronchitis. According to Prof. Molina, chronic bronchitis is essentially defined, by clinical standards, as a non-specific state of bronchial hypersecretion, possibly accompanied by functional respiratory disorders. The cited environment and heredity as possible factors in respiratory insufficiency.

Dr. Marcel Barjaud, a general practitioner and physician at the nearby spa, La Bourboule, considered cigarette smoking an important factor.

Chronic vs. Acute

Prof. Pierre Catilina, a leading professor of industrial medicine, asserted that a distinction should be made between patients who suffer chronic bronchitis as a result of heredity or repeated attacks of acute bronchitis during childhood, and smokers. He felt that smokers with abnormal coughs and morning catarrh could not be considered to have chronic bronchitis, even if they suffer from actual bronchial lesions, as such lesions are different from those described in textbooks. He stressed this distinction, pointing out that it relates to professional responsibility as well as preventive medicine.

Nevertheless, Prof. Molina asserted, smokers are a high-risk group, subject to infections and bronchial disease. At the outset, only the bronchi may be diseased, without ventilatory disorders, but it is possible that irreversible bronchiolitic lesions, responsible for functional respiratory disorders, are propagated by bronchial lesions in smokers, Prof. Molina said. He and Prof. Catilina agreed that there are two categories of lesions.

However, Prof. Molina said, isolated hypersecretion should alert the physician, because it fosters infections and could develop into respiratory insufficiency. Prof. Catilina expressed the certainty that, in this instance, smoking alone was not responsible. Only individuals subjected to additional risk-factors, such as those found in climatic work conditions, develop chronic bronchitis, Prof. Catilina said.

Dr. André Ledu, a general practitioner here, does not consider a smoker of 15 or 20 years, who coughs and expectorates, to have chronic bronchitis. He adheres instead to a criterion of

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Medical Tribune

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Experts Weigh Mammography Risk/Benefit

Medical Tribune Report

BETHESDA, MD.—A blue ribbon panel of cancer experts has urged the National Cancer Institute (NCI) and the American Cancer Society (ACS) to end routine mammographic screening of apparently healthy women under age 50.

In a hastily organized meeting at the Institute last month, Dr. Lester Breslow, head of the study group, said that while no direct evidence exists that the low level radiation used in screening mammography induces breast cancer, the potential risk to asymptomatic women under 50 outweighs the potential benefit of detecting breast cancer in its early stages. (Radiation doses 50 to 100 times higher than used in mammography have been linked to breast cancer.)

Dr. Breslow, Dean of the School of Public Health at the University of California in Los Angeles, made the recommendation at a meeting attended by directors of the NC-ACS-funded breast cancer detection demonstration program, representatives of the American College of Radiology and the FDA's Bureau of Radiological Health, the press and the public.

Approximately 260,000 women have enrolled in the screening program at 27 centers around the country since its inception in 1973, according to the ACS. Almost 130,000 are between 35 and 49 years old, the age group considered at risk by the study committee.

The group based its recommendation on an evaluation of the seven-year breast cancer screening project of the Health Insurance Plan of Greater New York (HIP), the prototype of the present program. No benefit was found in X-ray screening of women under age 50, but there was "certainly some hazard" from radiation exposure, according to Dr. Breslow.

Dr. Breslow's committee is one of three groups commissioned by NCI in October 1975 to evaluate mammography's benefits and risks following calculations by epidemiologists, primarily Dr. John C. Bailar, 3rd, editor of the *Journal of the National Cancer Institute*, that showed repeated exposure of women 35 to 50 years old to x-ray screening would result in as many lives lost to breast cancer as would be saved: a 1:1 benefit-risk ratio.

DR. BROSS

Recently, a leading U.S. cancer epidemiologist flatly predicted that the NCI-ASC program would result in a "nationwide epidemic" of breast cancer beginning in the 1980s.

"Starting 10 to 15 years from now, they're going to get in this group of women under 50 another 75 cancers, in addition to the 150 which would normally occur," Irwin D. J. Bross, Ph.D., told MEDICAL TRIBUNE.

Dr. Bross, Director of Biostatistics at Roswell Park Memorial Institute for Cancer Reseach, Buffalo, New York, calls routine mammographic screening a "mindless use of technology." "More than half of breast cancers can be picked up by physical examination, as the HIP study shows. And you don't cure every case that you pick up," he explained. "In mass screening, you're exposing 999 women to x-ray which is not helpful in order to catch that one woman in a thousand who has breast cancer. Mass screening of younger women is producing five or six new cases of breast cancer for each woman saved by early detection."

In the next few weeks, NCI will receive reports from the other two groups. One group, chaired by Dr. Arthur Upton, of the Department of Pathology, Health Sciences Center, State University of New York at Stony Brook, will review benefit to risk data in mammographic screening. Another group of pathologists, headed by Dr. Louis B. Thomas, Chief of the Laboratory of Pathology at NCI, will report on the histology of breast cancer cases discovered in the HIP study.

NCI and ACS will make a final decision on whether to drop women under the age of 50 from the program or to modify the procedures (perhaps as Dr. Bross has suggested, suspending centers with equipment that delivers more than 0.5 rad to each breast), based on these reports plus data submitted by the 27 screening centers.

However, the ACS said it is "extremely reluctant" to discontinue a program which is detecting early curable cancer in women under 50. Of the 129,000 women under 50 screened so far, 223 had breast cancer which was detected on the first examination. In 100 cases, the disease was detected by mammography alone, the Society said. And 79% of the cancers in these 29 women were caught before spreading to the lymph nodes, improving the women's changes for survival.

Tumor-Specific Antigen Tested in Lung Ca

PART II

Part I of this two-part series described the pioneering attempts by Drs. Thomas H. M. Stewart and Jules E. Harris, of the University of Ottawa, and Ariel C. Hollinshead, Ph.D., Professor of Medicine at George Washington University Medical Center, Washington, D.C., to develop and test an allogenic, tumor-specific antigen in the form of a vaccine that would be useful in the immunotherapy of lung cancer and possibly other cancers as well. Part II continues with more detail on the investigators' clinical strategy and experience.

By KRISTIN WHITE
Special Tribune Correspondent

"The number of patients we can treat with antigen is limited by the amount of antigen available, which, in turn, depends on the amount of tumor cells made available by other patients," Dr. Stewart told MEDICAL TRIBUNE. "Some lung cancers are only a few millimeters in diameter. That's enough, in time, to kill the patient, but not enough to yield much antigen. Each patient must give up his own tumor at the time of surgery, so we can later use antigen from it for somebody else." Dr. Stewart made the necessary arrangements for the patients in the study before they underwent lung surgery in various Ottawa hospitals.

The cells of each resected tumor are quickly frozen in liquid nitrogen and flown to Washington, D.C., where Dr. Hollinshead employs methods to peel the cell membranes from the rest of the cell material and solubilizes the membrane protein using low frequency sonication. If the tumor is large, it may be handled individually; small tumors of the same histologic type are usually pooled. Once in solution, the antigen is separated, purified, concentrated, and analyzed. In all, it takes from 10^8 to 10^9 cells to produce 20 mg of antigen, the strength of which may vary significantly from batch to batch.

The strength of the antigen is titered in the laboratory, and measured with skin tests on lung cancer patients in George Washington University Medical Center. "It would be wonderful to make one large batch of vaccine with standardized strength, and we're hoping to do this when large-scale tests are begun in Canada later this year," said Dr. Hollinshead.

The final product, which is flown back to Ottawa, is, in Dr. Stewart's phrase, "squeaky clean," and contains no living material of any kind.

Dr. Hiroshi Takita at Roswell Park Memorial Institute in Buffalo, N.Y., and Dr. Oleg S. Selawry at the University of Miami School of Medicine will be using antigen prepared by Dr. Hollinshead in upcoming studies which will attempt to duplicate the Ottawa results. A similar study by a number of Canadian institutions will also use Dr. Hollinshead's antigen, since the process is too complex and delicate to be reproduced elsewhere at the moment, and since a single source of antigen will ensure greater uniformity.

Dr. Stewart and Dr. Hollinshead hope that, in addition to confirming their findings, the forthcoming studies will help to refine the "engineering" aspects of the immunochemotherapy approach, and to establish the optimum dosages of the antigen.

Conservative Approach

"I'm sure there are more effective ways to use it," said Dr. Hollinshead, who points out that the amounts of antigen used in the Ottawa patients were deliberately low. "This study was meant to be the final step of the first phase of our investigations. We were doing the conservative thing, using proportionately much less antigen than we had been using in test animals, since we wanted to show only that the antigen would do the patients no harm. We were really pleased when, about halfway along, we saw that it was doing so much *good*."

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Na Thiopental May Reverse Brain Ischemia

Medical Tribune Report

PITTSBURGH—The anesthetic agent sodium thiopental has been shown in animal studies to protect the brain from neurological deficit when given as long as one hour after 16 minutes of global brain ischemia, a University of Pittsburgh researcher reported here.

"Based on our experiments, we think the primary insult to the brain is to a considerable extent... reversible," Dr. A. L. Bleyaert, of the Department of Anesthesiology said. "While monkeys are not human beings . . . there is some evidence in the literature that human beings have survived after long-lasting cardiac arrest, so we think these experiments are applicable," he told the Society of Critical Care Medicine.

In Norway, a patient who drowned in very cold water was successfully resuscitated after 45 minutes, Dr. Bleyaert noted, "and we ourselves had one, a four-year old child, who recovered after 20 minutes."

While his exact method has not been employed clinically in brain trauma or after cardiac arrest, the investigator stated, "Some anesthesiologists are using barbiturates during anesthesia or neuroanesthesia when there are hypoxic episodes, and have had unexpectedly good results. I can see this being used in patients after cardiac arrest as a regular thing, and this has already been carried out in some non-American centers."

Under the Pittsburgh study protocol, monkeys were subjected to 16 minutes of global brain ischemia by the use of a high pressure neck tourniquet. They were then given intensive care and monitored for seven days, before sacrifice. Thiopental was administered at 5, 30 or 60 minutes post-insult, in doses of 90 and 120 mg/kg of body weight, by intravenous infusion.

"Recovery in our treated group was remarkable, and appeared to be dose and time independent," he said. Neurological deficit in all the control monkeys ranged from 40% to 70% at the end of the study; in contrast seven monkeys treated with 90 mg/kg thiopental at five minutes postischemia had neurological deficit scores of less than 10% within 72 hours, and were essentially normal postischemia.

In the 30-minute group, three out of five recovered completely. Two did not recover to the same extent, but compared to the control group they showed "quite a good improvement." These results were essentially the same in monkeys not treated until 60 minutes postischemia, Dr. Bleyaert added.

"The ultimate degree of neurological deficit sustained," he suggested, "appears to occur as a result of the 'maturation' of the lesions in the brain after the initial ischemic insult. Therefore, prevention of this maturation process would ameliorate the development of postischemic encephalopathy.

"The development of the no-reflow phenomenon within one to two hours postischemia, which may be analagous to the maturation of the brain lesions, suggests that therapy should be started within this time period. Personally, I think that in humans there would be this possibility of recovery if the therapy is started within one to two hours. However, the earlier the start of therapy, the better the recovery expected."

Dr. Bleyaert said it is unclear how barbiturates protect the brain, but "reduction in $CMRO_2$ [cerebral metabolic rate of oxygen consumption] and stabilization of cell membranes are possible mechanisms of action."

Bicentennially Speaking

Just Who Was the Dr. Samuel Adams Who Signed the Declaration of Independence?

MEDICAL TRIBUNE's article (June 23) on the six liberty-loving physicians who signed the Declaration of Independence drew both praise and many inquiries from readers. (The Declaration signers were: Dr. Benjamin Rush, Dr. Josiah Barlett, Dr. Lyman Hall, Dr. Oliver Wolcott, Dr. Matthew Thornton, and Dr. Samuel Adams.)

Typical of these letters was the following:

"Your article was most interesting to me—an amateur student of early American history. For the ongoing Bicentennial madness it is most appropriate. I do want to question your facts, however. I cannot dispute that Rush, Hall, Bartlett and Thorton were physicians—the latter three by apprentice technique. Of those four, only Rush made a vocation of medicine while the other three were engaged in politics and planting (Hall).

"As to Adams and Wolcott, I believe you are in error and no source in my library can confirm your statement that either Sam Adams or Oliver Wolcott were, at any time, physicians. Adams was a graduate at Harvard and a lawyer—which profession he set aside to run a mill and other businesses left him by his father—he went bankrupt. Aside from political office he practiced law and died in Boston (not Bath, Me.) and resides in Old Gramercy Cemetery, Boston.

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Pregnant Despite Husband's Retrograde Ejaculation

Medical Tribune Report

LAS VEGAS—Voiding into the vagina directly after intercourse could be a practical and inexpensive alternative to artificial insemination for men with retrograde ejaculation, it was reported here.

Although the idea is repugnant to most women, those highly motivated to have children can easily overcome this objection, Dr. Joel D. Schram told the 32nd annual meeting of the American Fertility Society.

In the first reported case using this technique, a 27-year-old woman who had undergone 12 unsuccessful attempts at artificial insemination became pregnant, said Dr. Schram, Clinical Instructor in Obstetrics and Gynecology, University of Miami School of Medicine.

When first seen in 1973, she gave a history of an uneventful pregnancy five years earlier and subsequently tried to become pregnant without success.


DR. SCHRAM

Her husband, who underwent a Y-V plasty of the bladder neck in 1969 when 23 years old, was found to be a retrograde ejaculator with a sperm count of 83 million per cc.

During the following years, the woman saw several physicians and had artificial inseminations with the husband's semen specimen obtained by masturbation followed by gentle centrifugation to concentrate the sperm.

Despite the fact that her basal body temperature was normal, that she had regular 30-31 day cycles and that the semen specimens contained a fair number of sperm, she failed to become pregnant after 12 attempts.

Dr. Schram reasoned that since 30 minutes usually elapsed between ejaculation and insemination, perhaps it would prove helpful if the time lag was decreased by the husband voiding directly into the vagina as soon as possible after ejaculation.

On the day of planned intercourse at mid-cycle, the husband was instructed to restrict intake of fluids for six to eight hours before intercourse and to void immediately before.

He was able to void into the vagina 10-15 minutes after ejaculation.

When the woman was next seen, she had an eight-week pregnancy and went into spontaneous labor and delivered a normal 8 lb. 3 oz. girl 48 weeks later.

Although there are many uncertainties in the case, Dr. Schram feels that the method has advantages well worth considering in males with retrograde ejaculation.

It is not known if the patient was anovulatory intermittently or if further artificial insemination would have succeeded.

Neither is it certain whether the decreased time of contact increased sperm motility.

Dr. Schram believes that making the husband's urine more alkaline, by the ingestion of baking soda, might even be more effective than fluid restriction alone.

All of these factors may have to be weighed when attempting further trials of this regimen.

Induction of Labor Falling From Favor In Great Britain

Medical Tribune World Service

DUBLIN—Induction of labor is now falling out of favor with physicians in the British Isles where the practice was extended to more than half of all hospital births in some areas. Recent surveys have indicated that there is no real justification for the belief that induction decreases perinatal mortality, as its chief supporters have been maintaining for the last 10 years.

At Oxford University in England, where the induction rate has dropped from 56% in 1974 to the present level of 25%, the perinatal mortality rate remained at 9.4 per thousand, according to Dr. A. C. Turnbull, of Oxford, who pioneered the oxytocin method of labor induction. Essentially the same conclusions came from surveys of the perinatal mortality rate in Cardiff, Aberdeen, and in Dublin, he said at the joint meeting of the British and Irish Medical Associations here.

"Induction of labor can at best only reduce perinatal mortality in a relatively small proportion of cases, because the majority of deaths are due to causes not helped by induction, such as lethal deformity, extreme prematurity or placental abruption," Dr. Turnbull noted.

In a separate report, Dr. Kieron O'Driscoll, of Holles Street Hospital, Dublin, pointed out that inducing labor may actually affect the child's development after birth. Referring to the Cardiff study, he said: "The extended use of induction was associated with a fall in mean gestational age and in mean birth weights of infants born in the Cardiff area. This is an ominous finding which could have disastrous long-term implications for some children."

Both physicians said that they would be happy with an induction rate of about 10%, which is estimated to be about half the level of induction carried out in the U.S.A. and Canada.

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EDITORIAL CAPSULES

. . . brief summaries of editorials or comments in current medical and scientific journals.

"A Good Breakfast"

Nineteen seventy-five may be remembered in history as the year that for the first time there was no new case of smallpox in Asia. For doctors with no experience of this terrifying disease it may be difficult to appreciate the magnitude of the achievement of the medical services of countries in Asia, and the credit that is due to W. H. O. for providing them with leadership. Today only a small focus of smallpox transmission exists in remote and isolated regions of Ethiopia, and in a year or two the world may be rid permanently of one of the great pestilences of the past. Communicable diseases rightly remain one of the major preoccupations of W.H.O. . . .

". . . Only if national governments bring forward schemes based on the differing needs of their local communities can W.H.O. provide effective help. The immense technical skills and resources which W.H.O. now commands have to be harnessed. If local communities, and through them national governments, cannot or do not accept the challenge, then the irony of Francis Bacon will again be clear. 'Hope is a good breakfast, but it is a bad supper.' *(Editorial, The Lancet 1:1227, June 5, 1976)*

Gynecologist's Role

"Often the most severely ill patients in the gynecologic-obstetric suite are those who have had delayed referral for a complication.

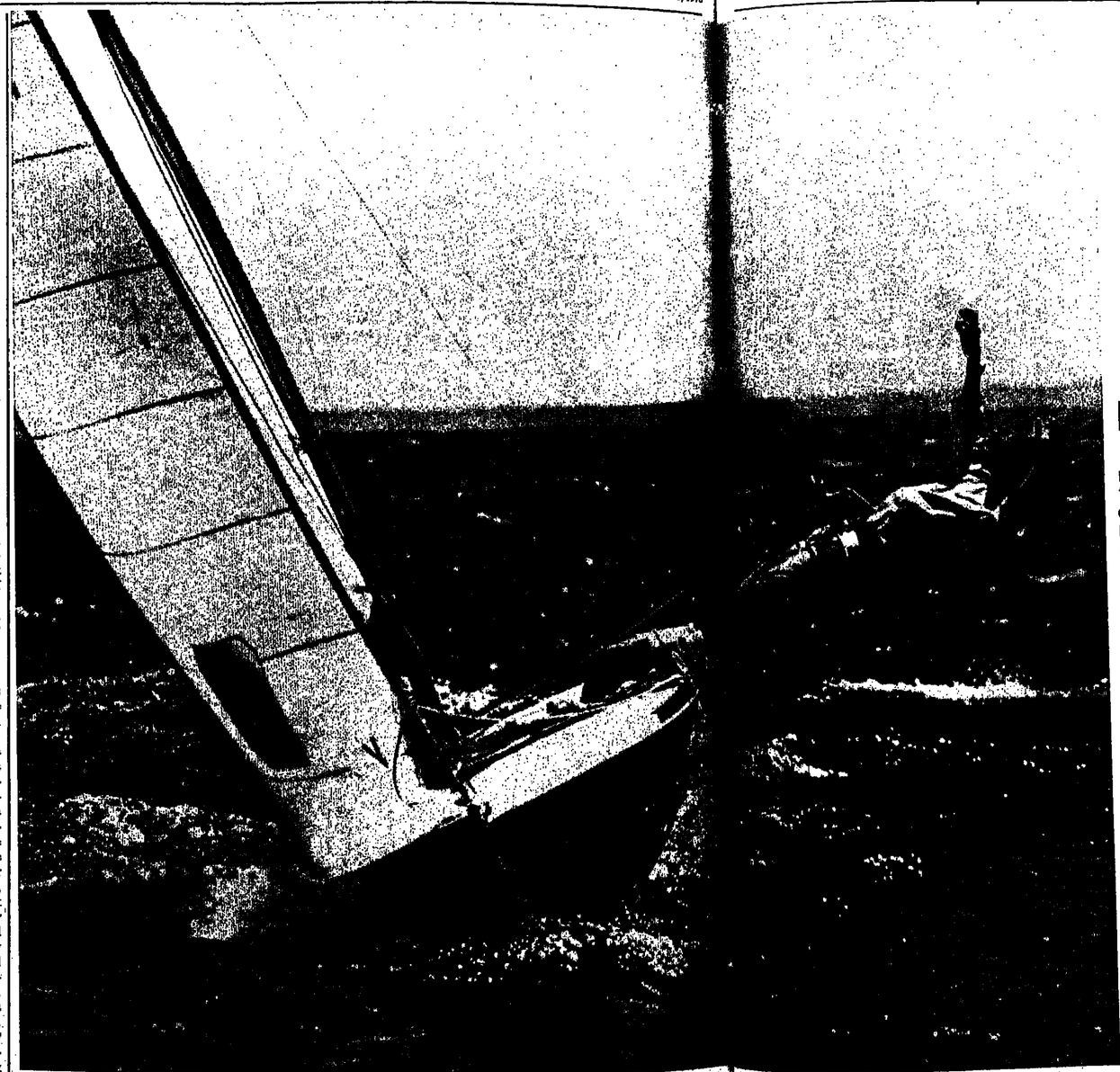
"Two recent theories of health care delivery would tend to aggravate this problem of late identification of complications. The first restricts the gynecologist to the role of consultant. The second visualizes him as a semi-administrative head of a large health care team, whose members presumably have less training and experience. In either instance the knowledge, experience, and skills of the gynecologist cannot be applied until a person with lesser training and experience has identified a problem. Though such systems may be necessary in some places, they tend to provide emergency rather than anticipatory or preventive medical care.

". . . many women have learned this lesson better than have health planners. By word of mouth within the family or among friends, they learn of the results to be obtained from continuing gynecologic care. Therefore, a large majority of women choose gynecologists as primary physicians, expecting to receive the medical care they need, or to be guided promptly toward that care . . ." *(Brooks Ranney, M.D., Obstet. & Gynec. 47:729, June, 1976)*

Report Window Falls

Medical Tribune Report

New York—A new amendment to the New York City health code makes it mandatory that physicians report all cases of persons under the age of 16 falling from windows.



Vitamin E Shown to Prevent Premature Aging of Human Cells

Medical Tribune Report

RENO, NEV.—Vitamin E has been shown to prevent "blow-outs" in human red blood cells, a signal that the cell is aging, Jeffery Bland, Ph.D., told an American Chemical Society regional meeting here.

Does this mean that patients may live longer or smooth the path to old age, by taking extra amounts of vitamin E? That's not definite yet, Dr. Bland said. But human studies conducted by him at the University of Puget Sound in Tacoma, Wash., have shown that "you should be able to avoid accelerated aging if you take the right amount," he announced.

Studies are now in progress to determine exactly what that "right amount" is, he also said. "Above a certain level, enhanced vitamin E ingestion can lead to a reduced ability in preventing erythrocyte membrane peroxidation, a weakened cell membrane, and a more rapidly 'aged' cell," Dr. Bland warned.

Process Slowed

In describing how the red blood cell is presumed to age, he noted that lipid peroxidation with the weakening of the cell membrane is caused by direct exposure to light or oxygen, or indirectly from the effects of smog, the sun, x-rays, or cigarette smoking. The result is a sort of "blow-out" called a budded cell. Vitamin E apparently slows down this process, caused by peroxidation of cholesterol, a component of the erythrocyte membrane itself, into cholesterol hydroperoxide, Dr. Bland said.

For example, in one study 24 human volunteers took 600 IU of α-tocopherol and then gave samples of their blood for comparison with nonsupplemented controls. "We were amazed to find that exposure of the cells to light and oxygen for 16 hours, conditions which in the absence of the vitamin E regime would have led to totally budded cells, gave only a small number of budded cells," Dr. Bland said.

In a second study, he and his colleagues exposed normal, random blood samples to light and oxygen in the presence of vitamin E. Again, "The cells resisted membrane destruction at the same rate . . . as the cells taken from those donors on the augmented vitamin E diet."

The vitamin is a "biological antioxidant" that "sits in the fatty bilayer of the cell membrane" as protection against the effects of cellular aging, Dr. Bland suggested. He recommended "enhanced intake" of vitamin E in the presence of environmental oxidants such as smog and cigarette smoking.

Surgeons Anti 'EM' Board

Medical Tribune Report

CHICAGO—The Board of Regents of the American College of Surgeons here has reaffirmed its position that "'emergency medicine' is not a medical specialty" and therefore "an American board of 'emergency medicine' should not be established."

IN CONSULTATION

What's New and Important About 'Slow' Viruses in Children

The Consultant

JOHN F. GRIFFITH, M.D.

Professor and Chairman, Department of Pediatrics, University of Tennessee Center for Health Sciences, and Medical Director, Le Bonheur Children's Hospital, Memphis, Tenn.

WHEN THE ASSOCIATION between measles virus and subacute sclerosing panencephalitis (SSPE) was first appreciated about 10 years ago, many wondered whether other viruses might produce similar or closely related diseases and whether the administration of live virus vaccines to young infants would result in an increased incidence of SSPE in future years. It is now clear that rubella virus can induce a similar clinical picture in the rare patient, usually 10 or more years after primary exposure to virus during congenital rubella infection. These patients develop signs of progressive central nervous system dysfunction; the diagnosis is verified by demonstrating rubella antibodies in the cerebrospinal fluid. Both this disorder and SSPE seem to occur in individuals with primary exposure to virus at a very young age.

It is now 13 years since the introduction of measles vaccine as a standard immunization procedure in the United States and rather than an increase in SSPE incidence, there has been a gradual decline in the number of new cases reported. It is too soon to know whether this is a permanent trend and, although tempting, it is certainly premature to conclude that measles immunization is playing a role in the changing incidence of the disease.

Progressive multifocal leukoencephalitis (PML) is the first demyelinating disease of man caused by a virus. The infecting agents, which have been recovered from the brains of these usually immunocompromised patients, are much more prevalent in the community than previously thought. Surveys of large populations of asymptomatic individuals indicate that from 50 to 70% of individuals, depending on age, have been infected with JC virus which is the papova agent most frequently recovered from patients with PML. Is it an example of an asymptomatic infection occurring at an early age which is activated later by interference with the host immune defense mechanisms? Or is it an acute infection occurring in an immunologically compromised host? These are the questions which researchers are currently examining and their answers should have practical import for the many physicians dealing with immunocompromised patients.

How do you define "slow virus" infections and what clinical entities would fall into this category?

The term refers to the tempo of a particular clinical illness which is relentlessly progressive following a prolonged incubation period lasting months to years. In addtion to SSPE, PML and chronic rubella encephalitis, which are examples of unusual infections with conventional virus agents, there are progressive "degenerative brain diseases" (Creutzfeldt-Jakob disease; Kuru) which can be transmitted to subhuman primates but which have not yet yielded detectable conventional virus nor resulted in the typical inflammatory or immunological responses associated with infection. Diseases involving other organ systems may eventually be explainable on a similar basis but to date the term "slow virus" of man refers only to slowly progressive, usually fatal disorders affecting the nervous system.

Does the herpes family of virus fit into the "slow" virus group? What are some of the newer concepts concerning the pathogenesis of herpes simplex virus infections?

Strictly speaking, the herpes viruses are not "slow viruses," yet their potential to produce disease months or years after primary infection justifies their inclusion in discussions of this subject. All the herpes viruses have the potential to remain latent in the human host after recovery from primary infection. Herpes simplex virus has been demonstrated both in sacral and trigeminal ganglia of patients at autopsy even though they had no overt clinical disease in life. Recurrent herpes simplex cervicitis is currently the second most common form of venereal disease and probably results from neural spread of virus from sacral ganglia to the periphery. In the same way virus introduced into the eye of a neonate born vaginally to an infected mother may reach the trigeminal ganglia and either remain occult or produce recurrent disease in the form of eye, skin or mucous membrane infection.

Have there been any treatments which have been successful for "slow" virus infections?

The course of SSPE has not been significantly altered despite intensive treatment efforts using corticosteroids, immunosuppressive agents, antimetabolites, irradiation, transfusion, and transfer factor. There are two case reports suggesting that cytosine arabinoside is beneficial for patients with PML, but this requires further documentation. At present, there is no satisfactory approach to the treatment of recurrent herpes infection other than superficial infections of the eye. In this instance, topical idoxuridine is effective even though it does not prevent recurrent infection.

What are some of the present theories regarding the pathogenesis of these clinical conditions? Is there any immunologic defect associated with these diseases?

The virus presumably becomes integrated with host cell genetic material following primary infection and remains in this quiescent state during the prolonged period of well-being preceding the onset of clinical disease. The factors of age at time of primary infection and physicochemical stimuli leading to "reactivation" in later years are prominent considerations in the theories of pathogenesis. Concurrent infection, with another virus, has also been mentioned as a possible factor contributing to disease production but as yet this is unproven. A part from the situation in PML where patients are usually immunosuppressed prior to the onset of symptoms, none of the other conditions have been associated with any demonstrable defect in host defenses.

What are the signs a general practitioner should be aware of in trying to make a diagnosis of "slow" virus diseases?

This disease category should be considered for any patient with a progressive dementing illness, particularly when associated with myoclonus and a CSF examination which is either normal or shows a slight mononuclear pleocytosis and a normal or borderline increase in protein with an elevated IgG content. SSPE and progressive rubella encephalopathy are suspected on clinical grounds and verified by detecting elevations in either measles or rubella antibodies in the CSF.

Husband's Device Enables Wife To 'Talk'

A light on the forehead helps this patient "talk" by indicating letters of the alphabet on the card held by her husband. A victim of amyotrophic lateral sclerosis, the patient is almost completely paralyzed, unable to speak. When only her neck muscles remained useful, the husband developed the device.

Next in Consultation

DR. MALCOLM S. ARTENSTEIN, Chief, Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, D.C., will discuss recent developments in the prophylaxis of meningitis and answer questions on the duration of protection of the polysaccharide vaccine, antigens involved in bactericidal reactions, tests useful in comparing vaccines, and the effectiveness of lipopolysaccharides as immunogenic substances.

Oral Zinc May Spur Wound Healing When Patient's Serum Zinc Is Low

Medical Tribune World Service

MONTREAL—Although recent evidence suggests that zinc plays an important role in nucleic acid synthesis, the addition of oral zinc to the diet for purposes of wound healing without demonstrating reduced serum zinc levels would be a vain endeavor, Dr. Warren E. C. Wacker, Professor of Medicine and director of Harvard's University Health Services, told a symposium here on zinc and copper.

On the other hand, normal zinc nutrition is essential for normal wound healing, he said. "The addition of zinc to the diet of patients with impaired wound healing who seem to be deficient on the basis of lowered serum zinc concentrations appears to be indicated," the investigator stated.

However, he faulted some reports of oral zinc supplements increasing the rate of healing in a variety of wounds including burns, stasis ulcers, decubitus ulcers and operative wounds in man: "Many of these studies have been uncontrolled and were carried out without benefit of an adequate analytical assessment of the state of zinc nutrition in the patients."

He emphasized that a super-normal zinc intake does not accelerate wound healing. Hence, the addition of zinc to the diet of patients with normal zinc concentrations is not warranted on the basis of present data.

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune
and Medical News
Published by Medical Tribune, Inc.

Control of Hyperglycemia

Laissons Laissez-Faire...

IT SEEMS PARTICULARLY APPROPRIATE that the recent major policy statement of the American Diabetes Association urging control of hyperglycemia and attainment of as near normal blood glucose levels as possible should have appeared with Dr. George Cahill, President of the American Diabetes Association, as its prime signatory. Dr. Cahill, Professor of Medicine at Harvard Medical School, also is President and Director of Research at the Joslin Clinic which has always staunchly championed the concept of strict control in management of diabetes.

A more laissez-faire approach has had many advocates. Danowski, two decades ago, in his survey, "Strict, Liberal and Intermediate Regimens of Diabetic Regulation," in *Diabetes Mellitus*, held that in the more laissez-faire approach "Asymptomatic hyperglycemia and glycosuria are accepted without concern, since it is felt that so-called complete control does not guarantee escape from the vascular complications of long-standing diabetes... Dietary restrictions are minimal... Normoglycemia and aglycosuria are considered as constituting either unnecessary precision of control or goals not attainable without dangerous shocking."

...Confusing the Issue...

It has indeed not been proven that "vascular complications of long-standing" are prevented by strict control; but one must distinguish between large vessel atherosclerotic complications where such proof has been sparse or lacking, and micro-angiopathy, lesions of retina and lens, nephropathy and neuropathy, where the evidence is clear that controlling hyperglycemia is efficacious. The failure to differentiate between large vessel and micro-angiopathy has confused the issue, misled the unwary, and confounded the diabetic-care debate.

Present knowledge does not afford truly effective means of preventing arteriosclerosis with or without diabetes. Nevertheless, control of hyperglycemia ought to be pursued for there are reasons to implicate it in large vessel arteriosclerosis although not as distinctly as in the genesis of micro-angiopathy. In the latter hyperglycemia leads to the intracellular accumulation of an inert *glucose metabolite*, sorbitol.

The prime lesion of arteriosclerosis is *lipid* of which the most visible vestige is cholesterol, rather than a glucose derivative. Yet it must be recognized that hyperglycemia leads to hyperlipidemia, and there are other ways in which sugar and fat metabolism interact. Insulin, in addition to its sensitive and immediate relationship with glucose, has a longer range and just as basic hormonal function, namely it serves as the anabolic energy storage lipogenic hormone.

...and New Insights

It is beginning to be increasingly considered that insulin, as a lipogenic factor, may lead not only to regulatory fat storage in its proper adipose depots, but in arterial subintima as well. Thus, paradoxically, insulin itself may be a pathogenic factor in arteriosclerosis.

It appears desirable from such considerations, evidence of which is still fragmentary, to keep serum insulin levels as well as glucose as low as is commensurate with performing necessary functions. Serum insulin levels are elevated in obesity and in maturity onset diabetes, particularly when dietary control is poor, in which circumstances large vessel atherosclerosis is accentuated. Since hyperglycemia is the prime stimulus to insulin secretion, control of hyperglycemia becomes important although for a less pathogenetically direct objective than in micro-angiopathy.

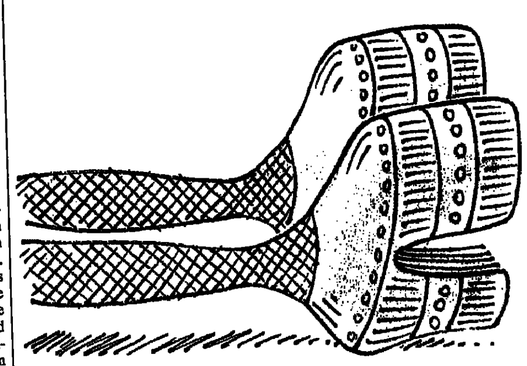
Evolving knowledge that defective cell surface receptor binding sites for insulin play a significant role in diabetes may lead to agents improving this defect, permitting greater insulin efficiency and accomplishment of its metabolic functions at a lower serum level. All the many new developments in glucose-insulin metabolism, their derangements in diabetes, and factors leading to long-term degenerative complications are consonant with the desirability of controlling hyperglycemia, the traditional view now reaffirmed by the American Diabetes Association.

R.S.G.

More On Soup and Materia Medica

A HALF YEAR AGO, an editorial on this page cited Dr. George E. Burch as recommending soup "to replace body fluids whenever possible" because it is an "infusion" of animal and plant tissue with essentially the same intra- and extracellular substances as found in the body fluids of man." The editorialist was certain that Mom's Chicken Soup merited this encomium.

Now Dr. Erwin Ziment in the July 12 issue of *JAMA*, in discussing expectorants, expresses the belief that "strongly flavored foods and condiments... have a significant effect on the bronchial glands, since many of these agents stimulate activity by the lacrimal, nasal, and salivary glands." Just add enough pepper and garlic and maybe even curry to chicken soup, he suggests, and *there* you may have the ideal treatment for bronchitis.



HELP!

LETTERS TO TRIBUNE

Just Who Was the Dr. Samuel Adams?

Continued from page 4

"Wolcott was the son of a Royal Governor and educated at Yale also as a lawyer and practiced law and held numerous offices for the crown prior to the Revolution.

"I would be grateful if you would check your facts and *allow* which of us is correct."

ELMORE W. LEWIS JR.,
Downey, Calif.

Oliver Wolcott's medical background was reported in MEDICAL TRIBUNE's stamp column by Dr. Joseph Kler (Aug. 4). Apprenticed to his brother who was a physician, Wolcott became an Army Surgeon only in the campaign against Burgoyne. He could be said to have abandoned medicine for a political career, ultimately becoming governor of Connecticut.

Samuel Adams was not, as Dr. Lewis believes, the Boston Samuel Adams who formed the Committee of Correspondence and was a major figure in organizing the Revolution. This is a common error; there are even displays of the portraits of the Declaration signers which make this error.

The Samuel Adams who signed the Declaration was a physician who was born in Connecticut in 1745. He lived most of his life in Massachusetts and Maine where he died Feb. 24, 1819. His diary, now in the New York Public Library, was considered "probably the most important and extensive medical diary extant of the 18th century and beginning of the 19th in the United States" according to historian Thomas M. Hunter. (See *U.S. Armed Forces Med. J.* 8:625, May, 1957.) He was for years the only physician in Bath, Me.

An intensive search for a portrait of Dr. Samuel Adams by several historical societies as well as by MEDICAL TRIBUNE failed. Therefore only his signature accompanied our story.

The original source for much of MT's article was *Harper's Encyclopedic History of United States*, a valuable but now out of print history published around 1900. *H.H.*

The Liberty-Loving Doctors

I want to commend you on your articles regarding the early American doctors [who signed the Declaration of Independence, MT, June 23]. I do not believe it is coincidence of the times, or education even, that brings out such a disproportionate leadership to freedom. Doctors, like no other professionals, realize the importance of non-interference in the carrying out of their duties and responsibilities to their patients. The practice of medical science, as all science, requires the atmosphere and reality of freedom, unencumbered by alien regulators. Something of this first hand awareness may very well have been what motivated those many doctors to respond to a threat to individual and cultural freedom.

MONTE HARRIS LIEBMAN, M.D.
Milwaukee, Wis.

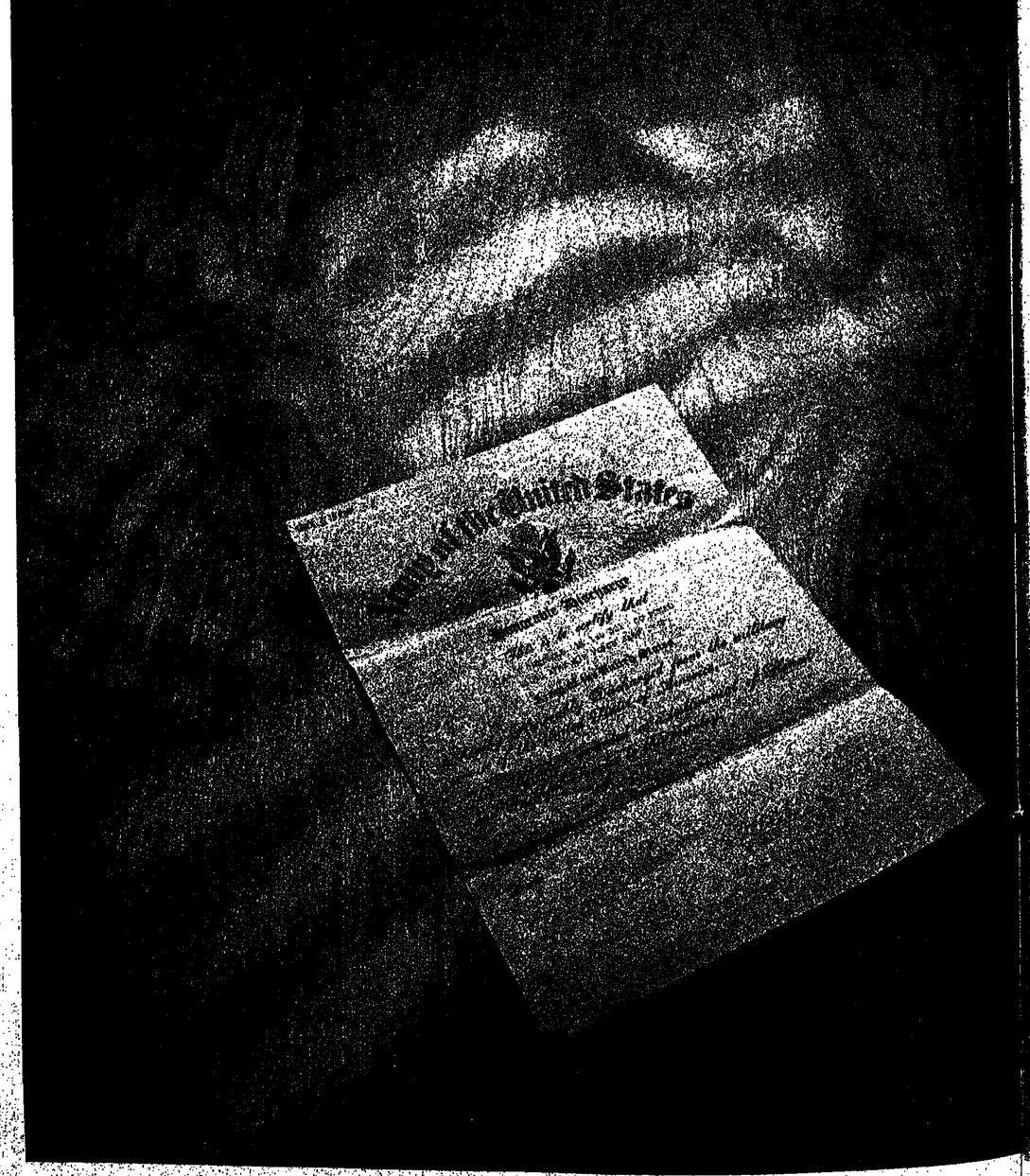
Re Antibiotics

Re the opinions and comments of Drs. Lasagna and Sackler on the use of antibiotics in common colds, I would like to add this little bit:

I have been in practice for thirty-five years and I have seen almost a negligible incidence of appendicitis and osteomyelitis and, in my humble opinion, this is due to the common practice of giving antibiotics to individuals, particularly youngsters. I also feel that among those physicians who administer antibiotics for common colds there is also a rarity in the number of pneumonias developing.

WALTER W. SACKETT, JR., M.D.
Tallahassee, Fla.

After 20 years, 523 veterans "re-enlisted" for a special assignment...



The assignment: combat hypertension

The VA studies showed it had to be controlled.

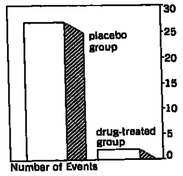
Long after World War II, large numbers of veterans were enrolled in what have since become known as landmark studies in the treatment of hypertension.

The VA studies[1,2] established that even moderately elevated blood pressure increases the risk of target-organ damage and death—and that hypertension should be treated in order to reduce morbidity.

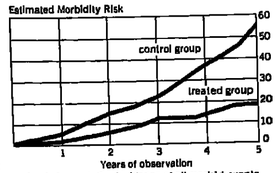
In the earlier study,[1] covering a two-year period, 143 male veterans with diastolic pressures averaging 115 through 129 mm Hg were randomly assigned to either placebo or active treatment. The study showed significant benefits to the drug-treated group.

The second study[2] covered a five-year period and involved 380 patients with milder hypertension (diastolic pressures averaging 90 through 114 mm Hg). Here, too, active drug treatment was beneficial; thus the estimated five-year risk of developing a morbid event was reduced from 55% to 18%.[2]

Morbid events in patients with diastolic pressures averaging 115-129 mm Hg. In the placebo-treated group, there were 27 morbid events, 4 of them fatal; in the drug-treated group, there were but two complicating events. (Adapted[1])



Estimated Morbidity Risk



Estimated cumulative incidence of *all* morbid events over a five-year period for patients with diastolic pressures averaging 90-114 mm Hg. (Adapted[2])

Control was achieved with:[1,2]

hydrochlorothiazide

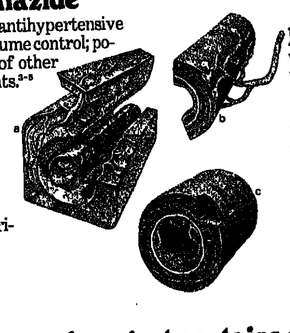
which provides a mild antihypertensive effect through fluid volume control; potentiates the activity of other antihypertensive agents.[3-5]

(a) Symbolized reduction in circulating fluid volume

plus hydralazine

the unique action of oral hydralazine lowers blood pressure through direct arteriolar vasodilation to reduce peripheral resistance.[3-5]

(c) Diagram of relaxed arteriole



plus reserpine

which lowers blood pressure through sympathetic inhibition;[3-5] also produces a central sedative effect which may prove particularly useful in the management of the stress-reactive patient.

(b) Schema of norepinephrine depletion at sympathetic nerve ending

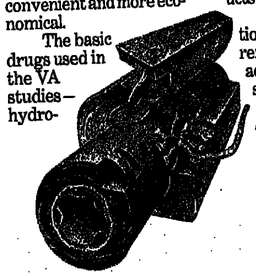
Only one antihypertensive agent contains all three components used in two published VA cooperative studies.[1,2]

In the VA studies, Ser-Ap-Es itself was not used. However, all the components of Ser-Ap-Es were used in varying combinations.[1,2]

Ser-Ap-Es contains all the antihypertensive medication many patients will need.

And when the dosage of each component corresponds to the dosage preestablished by individualized titration, Ser-Ap-Es may prove more convenient and more economical.

The basic drugs used in the VA studies—hydrochlorothiazide, reserpine, and hydralazine—are original products of CIBA research.



Note: Use Ser-Ap-Es cautiously in patients with advanced renal damage or cerebrovascular accident. Discontinue at first sign of mental depression.

Please turn page for brief prescribing information.

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

CIBA

References
1. Effects of treatment on morbidity in hypertension: Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967.
2. Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1152, 1970.
3. Russell RP: Hypertension, in Harvey AM, Johns RJ, Owens AH, et al (eds): *The Principles and Practice of Medicine*, ed 18. New York, Appleton-Century-Crofts, 1972, pp 331-334.
4. Gifford RW Jr: Drugs for arterial hypertension, in Modell W (ed): *Drugs of Choice, 1972-1973*. St. Louis, The CV Mosby Co, 1972, pp 390-393.
5. Sellers AM, Itskovitz HD, Lindauer MD: Systemic arterial hypertension, in Conn HL Jr, Horwitz O (eds): *Cardiac and Vascular Diseases*. Philadelphia, Lea & Febiger, 1971, vol II, pp 934-943.

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

WARNING
This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

INDICATIONS
Hypertension. (See box warning.)

CONTRAINDICATIONS
Reserpine: Known hypersensitivity; mental depression (especially with suicidal tendencies); active peptic ulcer; ulcerative colitis; electroconvulsive therapy.
Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

WARNINGS
Reserpine: Use with extreme caution in patients with a history of mental depression. Discontinue at first sign of despondency, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide. MAO inhibitors should be avoided or used with extreme caution.
Hydralazine: Hydralazine may produce in a few patients a clinical picture simulating systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to risk determination requires continued antihypertensive therapy with this drug. Symptoms and signs usually regress when the drug is discontinued but residua have been detected many years later. Long-term treatment with steroids may be necessary.
CBC's, L.E. cell preparations, and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine or if the patient develops any unexplained signs or symptoms.
A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.
Use MAO inhibitors with caution.
Hydrochlorothiazide: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.
Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.
The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy
Reserpine: The safety of reserpine for use during pregnancy or lactation has not been established; therefore, the drug should be used in pregnant patients or women of childbearing potential only when, in the judgment of the physician, it is essential to the welfare of the patient. Increased respiratory tract secretions, nasal congestion, cyanosis, and anorexia may occur in neonates and breast-fed infants of reserpine-treated mothers since reserpine crosses the placental barrier and appears in maternal breast milk.
Hydralazine: The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.
Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Thiazides cross the placental barrier and appear in cord blood.

Nursing Mothers
Thiazides appear in maternal breast milk.

PRECAUTIONS
Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or gallstones (biliary colic may be precipitated).
Exercise caution when treating hypertensives with renal insufficiency. Use cautiously with digitalis and quinidine.
Intraoperative hypotension has occurred in hypertensive patients receiving rauwolfia preparations, but withdrawal of reserpine does not assure that circulatory instability will not occur in such patients.
Hydralazine: Use cautiously in suspected coronary artery or other cardiovascular disease, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.
Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.
Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.
Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.
Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.
Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.
Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver diseases or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.
Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.
Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS
Reserpine: Gastrointestinal—hypersecretion; nausea; vomiting; anorexia; diarrhea. *Cardiovascular*—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. *Central Nervous System*—drowsiness; depression; nervousness; paradoxical anxiety; nightmares; rare parkinsonian syndrome and other extrapyramidal tract symptoms; CNS sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, and optic atrophy). *Miscellaneous*—frequently nasal congestion; pruritus; rash; dryness of mouth; dizziness; headache; dyspnea; syncope; epistaxis; purpura and other hematological reactions; impotence or decreased libido; dysuria; muscular aches; conjunctival injection; weight gain; breast engorgement; pseudolactation; gynecomastia; rarely water retention with edema in hypertensive patients.
Hydralazine: Common—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent*—nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.
Hydrochlorothiazide: Gastrointestinal—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo, paresthesias, headache, xanthopsia. *Dermatologic-Hypersensitivity*—purpura, photosensitivity, rash, urticaria, necrotizing angiitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. *Hematologic*—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. *Cardiovascular*—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. *Other*—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSAGE
As determined by individual titration (see box warning).
Usual dosage is 1 or 2 tablets t.i.d. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.

HOW SUPPLIED
Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 30, 60, 100 and 1000.
Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

2/5049 17

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

...brings three modes of action to bear on hypertension

CIBA

Tumor-Specific Antigen Aids Recovery from Lung Cancer

Continued from page 3

In the past, some investigators sought to innoculate patients with ground-up, frozen, or irradiated whole tumor cells, but the results were disappointing. Dr. Stewart and Dr. Hollinshead discovered some of the reasons why.

"A tumor cell contains much more than tumor-associated antigen," Dr. Hollinshead said. "It also contains organ antigen, which, of course, if used in the vaccine might induce destruction of normal tissue. There are also 'blocking factors,' which I prefer to call 'inhibitory factors,' which inhibit the effectiveness of the tumor antigens. Furthermore, there may be enhancement factors, which encourage the growth of tumor cells. We know such factors exist in animal cancer cells, and they could very well exist in human cancers."

No Easy Task

In order to infiltrate the target area with tumor-killing lymphocytes, without harming healthy tissue, the obvious, though by no means easy, approach is to use tumor antigen alone, as Dr. Stewart and Dr. Hollinshead have done.

While their work is far from anecdotal, the two doctors did not work with very many patients and, with limited funding, were forced to proceed slowly. "This was no disadvantage, in fact, we were able to pay careful attention to important ancillary questions which might have been overlooked in a large-scale study," Dr. Hollinshead says.

"We studied and measured the amounts of inhibitory substances in each individual tumor, and compared the amounts present in the different types of lung cancer," says Dr. Hollinshead. "We found that the small cell (oat cell) type contains enormous quantities of inhibitory factors, which helps to explain why these tumors are so fast-growing and so dangerous. The epidermoid (squamous) cells have much less inhibitory material, while the adenocarcinomas contain an intermediate amount. This is all relative, of course—compared with leukemia, where much smaller amounts of these substances are present, all types of lung cancer are pretty bad."

Dr. Hollinshead also studied four antigens which are associated with human fetal lung tissue. These disappear in normal adult lung tissue, but reappear on the surface of epidermoid lung cancer cells. "But the surfaces of small cell carcinoma of the lung appear to have no fetal antigens, while two of these antigens appear on the surfaces of adenocarcinoma. This kind of information is quite important, and may eventually help us to understand the nature of the different types of cancer. They seem to be vastly different.

"We need to understand the differences and to exploit them wherever possible. 'Exploitable difference' is a term that we like to use—so far as Dr. Stewart and I are concerned, it's the name of the game."

It will be at least three years before immunochemotherapy will be of use to large numbers of lung cancer patients, Dr. Stewart emphasizes. "It will take that long to complete final studies, assuming that all goes well in the meantime," he said.

In any event, the treatment strategy is likely to be effective only with patients whose lung cancer is operable, since the immune system appears to be ineffective against a mass of tumor. The gross tumor must first be eliminated by surgery, and vigorous adjuvant chemotherapy must be used to attack remaining cells and imperceptible metastases. Then, stimulated by the chemotherapy and reinforced by allogeneic antigen, the immune system, in theory at least, should be able to handle surviving cancer cells.

Vials of experimental lung cancer vaccine, prepared by Ariel C. Hollinshead, Ph.D., of George Washington University, are received for clinical use by Drs. Thomas H. M. Stewart and Jules E. Harris, of the University of Ottawa.

New Tests Help Dx, Rx of Multiple Sclerosis

Continued from page 1

may prove to be the first test available that can specifically detect multiple sclerosis. It has apparent advantages over tests which measure elevated IgG levels in cerebrospinal fluid (CSF) in that it uses blood instead of CSF, takes less than four hours to complete, and gives more reliable results.

The therapy monitoring test, a radioimmunoassay, determines the degree of activity of multiple sclerosis by measuring the amount of myelin basic protein in CSF. The protein is found in the CSF of many patients with the disease but seldom in patients with other neurologic disorders. Concentration of the protein rises as the disease progresses from an inactive to an acute stage. The protein level should fall as the disease subsides if drug therapy is effective.

In the diagnostic test, peripheral blood lymphocytes from patients with multiple sclerosis exhibit an increased capacity to adhere to human epithelial cells persistently infected with measles virus, according to Dr. Nelson L. Levy and associates from the division of immunology of Duke University Medical Center.

Rosette Patern

Lymphocyte adherence to measles-infected cells was studied in 27 patients, aged 22 to 51, with multiple sclerosis of varying severity, activity and six months to 20 years duration, and in 36 controls who were either healthy or had some neurologic or non-neurologic disease other than multiple sclerosis.

Lymphocytes from multiple sclerosis patients formed a rosette pattern around a mean of 69% of measles-infected cells compared to a mean of 28% in controls, the team noted. However, of direct clinical value, the researchers stressed, is the absence of any overlap between values of the multiple sclerosis and control groups.

Severity, duration and degree of activity of multiple sclerosis had no effect on the degree of rosette formation. However, the researchers did observe that lymphocyte adherence was higher in black individuals than in whites, in both the control and multiple sclerosis groups. Consequently, the team considers values above 55% in whites and above 60% in blacks to be abnormal.

Co-authors of the Duke University report (*New Engl. J. Med.* 294:1423, June 24, 1976) were Paul S. Auerbach, A.B., and Edward C. Hayes, Ph.D.

The test developed at Johns Hopkins is clearly not diagnostic of multiple sclerosis, Steven R. Cohen, Ph.D., a postdoctoral fellow in biochemistry, emphasized in his report to a recent meeting of the American Neurological Association in San Francisco. Its best application, he suggested, would be in monitoring therapeutic response. By measuring changes in demyelination activity, the new radioimmunoassay indicates changes in the severity of the disease process.

Dr. Cohen performed the assay on a total of 210 patients, all being treated at Johns Hopkins. Of these, 23 patients had multiple sclerosis in varying degrees of severity, 184 had non-demyelinating neurologic diseases, and three had myelinopathies.

Test results among the multiple sclerosis patients fell into three ranges, he found. Ten of them, in whom the disease was inactive, had negative results in the range of 0 to 10 ng/ml. Seven patients with "slowly progressing" multiple sclerosis had results in the 10 to 20 ng/ml range that Dr. Cohen described as "weakly positive." And six of the patients, in acute stages of the disease, had "very positive" test results in the range of 20 to 100 ng/ml.

Serial Samples Vary

In one of the multiple sclerosis patients, Dr. Cohen said, serial samples were obtained two weeks before acute exacerbation, during the exacerbation, and two weeks later. The values of myelin basic protein were 8, 60, and 6 ng/ml, respectively.

The test was positive, greater than 20 ng/ml, in only three of the patients with non-demyelinating neurologic disease, Dr. Cohen reported. Two of these had just suffered acute strokes and the third was alcoholic, he said.

The three patients with active demyelinating disease also had positive results, Dr. Cohen said. One had transverse myelitis, one had metachromatic leukodystrophy, and one had a hereditary leukodystrophy.

The test, using 20-fold concentrated CSF, is sensitive to 2 ng/ml at present, Dr. Cohen noted, but he hopes to refine it further and make it sensitive down to the picogram range which should make it possible to use urine or plasma instead of CSF.

Measuring Capillary Blood Flow

Non-invasive laser flow monitor measures capillary blood flow rate by noting shifting wave frequency of light scattered by red cells. Device can screen new drugs for circulatory effects and monitor shock or vascular disease therapy, says Dr. Michael Stern, of the National Institutes of Health.

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Swine Flu Vaccine Safety Inferred From Field Trials, Past Experience

Continued from page 1

"idiosyncratic occurrences" could be encountered with the controversial swine-type flu vaccine, and that assurances of long-term safety were based on the judgments of past experience.

Noting that in field trials of the flu vaccine in 5,000 persons there was only a 1.2% incidence of febrile reaction, Dr. Cooper stated that a warning of a "few severe side effects" had been issued by the Public Health Services Advisory Committee on Immunization Practices. "These side effects would be limited to possible severe egg reactions," Dr. Cooper said. As for the incidence of reactions in older people receiving the bivalent vaccines, Dr. Cooper put them at a maximum of 2%. He said constitutional symptoms were set at between 5 and 6%.

'Adequate Assurances'

Asked by Dr Sackler whether the decision for the vaccination program did not bypass the chronic toxicity data generally required for drugs, Dr. Cooper responded, "The same body of data covering past experience in using influenza vaccines and our vast knowledge of the behavior of the virus during natural pandemics provide adequate assurances that there is no chronic toxicity problem involved with this vaccine.

"In contrast," Dr. Cooper continued, "drugs usually contain ingredients which are completely foreign to the body, either as naturally occurring contaminants or as part of pharmaceuticals. Long-term toxicity studies are more likely to be required for these agents because our in vitro data is far more limited, if not nonexistent, and the drugs themselves are more apt to be used on a long-term basis, whereas vaccines are not administered repetitively over long periods."

Dr. Cooper categorically stated that there was no indication of cancer or birth defects as a result of either the influenza pandemic or the proposed vaccines.

On the liability issue, the government official said that pending federal legislation "would allow us to indemnify the manufacturer's from claims arising from the inoculation with the vaccine."

He added, "It would not cover claims arising from negligence on the manufacturer's part, however." Dr. Cooper also said that HEW did not have a position on whether or not the government should provide direct liability coverage.

"We have said that we will be responsible for the testing of the vaccine to assure safety and effectiveness and for adequately informing the recipients of the vaccine of its benefits and risks," Dr. Cooper declared.

Continued Next Issue

Swine-type flu vaccine gun is tested during a training session for 40 southern California health workers by Julie Kalnas, an immunization specialist. The high pressure gun is capable of vaccinating nearly 1000 persons per hour.

Encouraging Results Seen in I^{125} Treatment of Prostate Cancer

Medical Tribune World Service

VANCOUVER, B.C.—Encouraging results with treatments for prostate cancer which utilize I^{125} seeding or x-irradiation via linear accelerator were reported here at a symposium on radiation therapy.

Survival rates in some 200 patients who had seeds containing I^{125} implanted in their prostate glands "are as good as those of alternative methods of treatment of corresponding stages of the disease, and the quality of life post-treatment seems as good or better than that achieved with any other active therapeutic program for comparable stages," declared Dr. Willet F. Whitmore, Chief of the Urology Service, Memorial Sloan-Kettering Cancer Center, New York. The overall actuarial five-year survival rate for the patients in this series is 80% with "good local control and excellent function," Dr. Whitmore told MEDICAL TRIBUNE.

The series consisted of patients in Stage B, having apparently localized tumors, and Stage C, those with extracapsular extension, Dr. Whitmore said, adding that it is difficult to make direct comparisons with other regimens because of different criteria for patient selection.

Implantation of the .5 millicurie seeds, performed simultaneously with bilateral pelvic lymph node dissection, has had a "mild" physical impact, Dr. Whitmore said, with a postoperative hospital stay averaging eight days. The isotope has a half-life of one year, and delivers at least 16,000 rads in a year, 8,000 of them in the first two months.

More than half the patients showed palpable evidence of regression within one year, he continued, and more than three quarters within two years. But about 60% of those patients with demonstrable regional lymph nodes at operation will have bone metastases at two years.

X-irradiation, using a linear accelerator, has achieved direct, disease-free survival of 70% at five years and 42% at 10 years in Stage B patients, reported Dr. Malcolm A. Bagshaw, Professor and Chairman, Department of Radiology, Stanford University School of Medicine, whose team has treated more than 430 Stage B and C patients in the past 20 years. Direct, disease-free survival in patients with extracapsular extension has been 36% at five years and 29% at 10 years.

These survival figures compare with 80% five-year survival after surgery and 50% at 10 years, Dr. Bagshaw told MEDICAL TRIBUNE. However, he noted, irradiation maintains potency in at least 50% of patients and causes relatively few urinary complications, whereas surgery is accompanied by a 5 to 15% incidence of urinary incontinence and 100% impotence. Irradiation damage to the bowel has a low incidence, he added.

Currently, Dr. Bagshaw said, the Stanford group is trying to accomplish two goals. One is to prolong survival in Stage C patients. Using staging laparotomies, the team has found that about a third of patients with apparently localized cancers have metastases to the pelvic lymph nodes, so the irradiation fields have been extended.

The other goal, he said, is to persuade primary care physicians to perform rectal examinations to detect prostate cancer early. Although prostate cancer is considered an old man's disease, he said, he is seeing patients in their 50s and even in their 40s.

VA Launches Study of Prostate Ca Therapy

Medical Tribune World Service

VANCOUVER, B.C.—The launching of a Veterans Administration study designed to evaluate the relative benefits of radical supervoltage radiation therapy, versus radical prostatectomy in localized prostatic cancer and the relative effectiveness of radical radiotherapy versus delayed endocrine therapy (1.0 mg DES) in more extended malignancy was announced here at a meeting of the American Radium Society by Dr. Bernard Roswit, Chief of the Radiation Center at the Bronx VA Hospital and Associate Professor of Radiotherapy at the Mt. Sinai School of Medicine, New York City.

The $1 million study, to be financed by the National Cancer Institute, plans to enroll 150 Stage B patients, those whose disease is limited to the prostate and considered operable, and 1500 Stage C patients, those with extracapsular extensions and considered inoperable, Dr. Roswit said.

Twelve large VA hospitals are already in the study, and the Surgical Chairman, Dr. David Paulson, of Duke University, will invite non-VA institutions to participate.

Ileo-Jejunal Bypass Effective Despite Exposure to Risks

Medical Tribune World Service

DUBLIN—Ileo-jejunal bypass can remove as much as 150 lbs. from the morbidly obese patient—but it can also expose him to risks ranging from troublesome infections to death. Those conclusions came from a survey of 100 patients who had undergone the controversial operation in England over the last few years, according to Dr. John Gazet, of St. George's Hospital, London.

Based on the survey, a mortality rate of about 4% can be expected following ileo-jejunal bypass, Dr. Gazet told a joint meeting of the British, Canadian and Irish Medical Associations. Before death, two patients became extremely debilitated from vomiting and diarrhea, a third had a ruptured abdomen and a fourth developed acute cholecystitis, he explained.

In addition, 26 of the 100 patients developed surgical complications including sepsis associated with abdominal wound hernia, ruptured abdomen, chest infections, deep vein thrombosis leading to pulmonary embolism, and small bowel fistulae, Dr. Gazet said, noting that other patients developed late complications such as tuberculosis, meningitis, malabsorption syndrome, hemorrhoids and fatty liver.

Not Below 220 lbs.

The English surgeon stressed that in spite of complications "which should not be minimized," ileo-jejunal bypass is frequently the most effective option for patients who weigh from two to three times more than they should for periods of five years or more. However, he added that it should never be applied to patients who weigh less than 220 lbs.

Weight loss six months after the operation ranges from 13 to about 150 lbs. following various modifications of the bypass procedure, and usually stabilizes close to or slightly above normal weight from two to four years after.

Weight loss seems to result from the digestive discomfort caused by the operation itself, Dr. Gazet said. If the patient eats too much, he vomits; if he drinks excessively, he gets diarrhea. Eventually the patient learns to live with the threat and eats and drinks at a level where discomfort is minimized.

Special Camp Brightens Lives of Hemophiliacs

Self-injections of factor VIII are part of the campers's training, as shown by 14-year-old Jeff Gannon. "I guess I'd rather do it myself," said Jeff. "I know when it hurts and at the hospital they don't."

Camper tries his hand at archery as Freddie Dennis, a staff member who is also a hemophiliac, keeps watch.

CEDAR LAKE CAMP in Michigan is teaching youngsters how to hit the bull's eye, paddle a canoe—and how to infuse themselves with factor VIII. The campers are all boys with hemophilia or girls with Von Willebrand's disease, and the camp has had "a major impact on our lives," according to some veterans. Sponsored by Hemophilia of Michigan, a nonprofit organization, and the University of Michigan Hospital, the camp is filled to capacity this year with 167 campers, from as far away as Belgium. The 45-member camp staff stresses independence, teaching the kids about the nature of their disease, and how to take care of themselves. A three-week camp may require as much as $30,000 worth of factor VIII, the blood component used to treat pain and stiffness due to joint bleeding, the major complication of the disease. For this and other needs, the camp infirmary is staffed around the clock, under the direction of Dr. John Penner, Professor of Internal Medicine at UM. If adequate funds are available, the camp will add a long-range genetic counseling program. However, it has already proved useful in helping these children lead their own lives. As one staffer put it, "That's the point: to let the campers be kids with hemophilia, rather than hemophiliacs first and last."

Group living gives the campers a chance to see that others with the same problem can take care of themselves. "One parent said that her kid was a complete hypochondriac before coming here," a staff member noted. The children also learn to socialize.

Swimming is important for hemophiliacs, as water relieves pressure on painful joints. Some campers have gone on to join high school swimming teams. Beginner gets help from physical therapist Bev Hudson, right.

The crafts building offers a change of pace for campers who may be suffering from painful joints caused by bleeding. Cost to families is only $50 a week.

Pediatric Progress

. . . presenting excerpts from current journal articles and commentaries of interest to physicians who treat children.

Pediatric Hypertension

"Surveys of patients at three pediatric teaching hospitals showed a low percentage of blood pressure recordings by the examining physician in the walk-in or emergency clinics. The frequency of blood pressure measurement was higher among inpatients, especially on medical services. A recommendation for obtaining blood pressure measurements is made on three bases: (1) many patients use these ambulatory services as their major source of care, (2) many conditions for which care is sought and many therapeutic agents are associated with hypertension, and (3) unless measurements of blood pressure become customary during training, it is likely that blood pressure recording may not be included as part of routine physical examinations." *(Patricia T. Pazdral, M.A., et al, JAMA 235:2320, May 24, 1976)*

Teratogen: Alcohol

". . . by 1980 there will be 1½ million alcoholics in Britain. . . . One aspect which has received little attention is the effect of alcohol on the offspring of mothers who drink heavily during pregnancy. A well-controlled prospective study now convincingly displays the handicaps, both physical and mental, that maternal alcoholism may impose on the developing fetus.

"Each alcoholic mother was well-matched by two controls; 4 of the 23 offspring of mothers classified as heavy drinkers died within one week of birth —a perinatal mortality of 17% against 2% in the controls. In 44% of the surviving children of alcoholic mothers the I.Q. was below 80, against 9% in the controls. Intelligence apart, 32% of the survivors showed a spectrum of abnormal physical features which suggest the existence of a true fetal alcohol syndrome; none of the controls had these features.

"A characteristic of the disorder is growth deficiency. The babies are short for weight rather than light for length and their lineal growth rate is only 65% of normal; average weight gain is less than 40% of normal despite an adequate caloric intake. The children all had short palpebral fissures, and many also had microcephaly, cardiac septal defects, and joint anomalies ranging from congenital dislocation of the hip to flexion and extension disabilities. At necropsy the brains of affected neonates have shown extensive developmental defects . . .

"To date, very few environmental agents have been indicted as human teratogens. We now know that heavy drinking in early pregnancy endangers the fetus. The dysmorphogenic effects of alcohol should be widely publicised; and serious consideration should also be given to termination of pregnancy in mothers with chronic severe alcoholism who have continued to drink..." *(Editorial, The Lancet 1:1335, June 19, 1976)*

'Accurate' Device Gauges Maturity of Fetal Lungs

Continued from page 1

An automatic analyzer identifies the lecithin-to-sphingomyelin ratio in the fluid sample when the latter is exposed to a temperature of 24°C. The resulting figure is known as the P ratio.

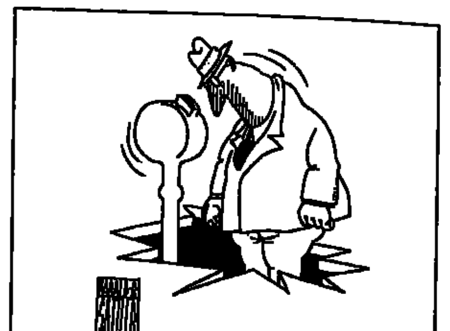
"During gestation the P value decreases steadily from about 0.4 to 0.2 and the value of P at 0.310 has been tentatively assigned to the upper limit threshold above which respiratory distress syndrome may develop," Dr. Serr observed.

He noted that the device offers an advance in implementing current obstetric philosophy which tends to place less emphasis on gestational age and weight, and far more on fetal lung maturity in determining when to start induction in a complicated pregnancy.

Currently available methods for measuring fetal lung maturity, he said, are "either cumbersome and time-consuming, or coarse and inexact. By contrast, the new device is highly accurate, requires no highly specialized training to operate or interpret, and can be installed in any delivery room or physician's office."

Dr. Serr said that he foresaw other possible applications than in complicated pregnancies. He cited, as one instance, the situation in which the date of term is uncertain: if the fetus is large for its presumptive age, the physician may induce labor only to find that the neonate has immature lungs and RDS. The new device, said Dr. Serr, would preclude such errors.

The instrument is currently undergoing clinical evaluation in several European centers and in one American institution, he stated.



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Current Opinion

On Character Assassination

By EDGAR END, M.D.

Assistant Clinical Professor of Environmental Medicine, Medical College of Wisconsin, Milwaukee, Wisc.

"The thing that hath been, it is that which shall be;
And that which is done is that which shall be done:
And there is no new thing under the sun."
—ECCLESIASTES

LONG AGO, while being admitted to an allied sciences membership in the International College of Surgeons at a meeting in Chicago, I heard an address by a distinguished English surgeon whose remarks are very relevant at this time. He told how the current English health system was foisted on the English people. According to him, the whole idea was initially rejected by the English people because of their high regard for their physicians. The government then backed off in an appearance of deference to the wishes of the electorate. Actually, however, they were merely regrouping their forces. Since the respect of the people for their physicians had prevented the passage of legislation, the government began an insidious and finally successful plot to break down this relationship. They did this in many ways, but perhaps their most effective method was to publish unweighted data on the annual income of the highest bracket medical specialists. The final result was, of course, to portray the English doctor as an avaricious and unprincipled individual. As soon as this was accomplished, parliament found little resistance to the passage of national health insurance.

Today we are surely witnessing the same insidious activity on the part of government and the news media. Large payments by Medicare to groups of physicians are publicized as being paid to the titular head of the group; exorbitant awards in malpractice cases have not only resulted in astronomical increase in malpractice cost but leave the inevitable impression that the harm being done to patients by doctors must be incredible if it is punished by such astronomical awards; sincere self-policing studies by surgical groups are given wide publicity and inevitably portray the surgeon as a bungling, money-mad slasher; and over emphasis of the side effects and alleged dangers of medications inevitably involves the physician who administers or prescribes them. The ultimate result of this many-pronged attack on the image of the physician must surely be a calculated one.

We have no English nobleman to point out this unwarranted attack for the type of character assassination which it is, but we do have MEDICAL TRIBUNE, which enjoys the esteem of the medical profession and the respect of the public. If you believe, as I do, that this concerted attack on the image of the American medical profession is a repetition of the method by which the English people were "sold" on national health insurance, I urge you to call the attention of your readers to this fact. Your acceptance of this challenge and responsibility might well be the most important effort that any one individual or group of individuals can mount in the fight against government invasion of the medical profession.

Kidney Transplants and Ca

Medical Tribune World Service

HAMBURG—About one out of every four patients who received kidney transplants from five to 10 years ago may develop skin cancer or other malignancies, according to a recent survey compiled by Dr. James May and his colleagues of the R.P.A.F. Medical Center in Sidney, Australia. The overall cancer incidence observed in 1843 patients from Australia and New Zealand who received one or more kidney transplants between 1963 and late 1975, ranged from 8 to 25%, depending on the length of the transplant period, he told the 12th International Congress of the European Dialysis and Transplant Association here.

Dr. May warned that it may be necessary to withdraw the immunosuppressive drugs which are designed to insure that the kidney graft is not rejected, but which at the same time may leave the patients more susceptible to cancer.

Wheelchair Olympics

Former Alexandria, Va., high school football hero Gerry Bertier, paralyzed from auto crash, hefts shot in preparation for Wheelchair Olympics, held in Toronto this month. He tosses shot 23' and discus 66'.

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Dr. Shumway's Stanford Team Completes 100th Heart Transplant

By HARRIET PAGE
Special Tribune Correspondent

STANFORD, CALIF.—The heart transplantation team here at Stanford University Medical Center recently implanted a new heart in their 100th patient. MEDICAL TRIBUNE asked Dr. Edward B. Stinson, who is now in charge of the program, to comment on their experience to date and their expectations for the future. (Dr. Norman Shumway, Chairman of Stanford's Department of Cardiovascular Surgery, remains the principal investigator for the program. Dr. Stinson, an Associate Professor in the department, has performed most of the operations.) The interview with Dr. Stinson follows:

What is the present status of heart transplantation? How many transplantation procedures are being done?

Right now, Stanford's program is the only consistently active, clinical heart transplantation program extant in the world. It's being performed sporadically at about five other centers scattered around the world. But we perform an average of one transplant procedure every three weeks, or about 20 a year. This represents a slight but significant increase in activity compared with four or five years ago, and the survival rates are also increasing. In 1968, for instance, when we first began this project, the survival rate for one year was 22%. In 1970 it reached 50%. Now, the expectation for surviving at least a year after heart transplantation is 60%. The long range survival rates of course are lower because of complications associated with the immunosuppressive medications that are necessary. But on the basis of our current statistics, the predicted five-year survival rate is about 40%. And 90% of these patients who survive for a year or more after operation are rehabilitated. They're free of cardiovascular symptoms, and the majority of them who were actively employed up to the time they became severely ill have returned to work. So there is a true degree of rehabilitation associated with this procedure, and we're still excited about it.

Will you step up your program?

We are expanding our areas of investigation in heart transplantation, and we plan to expand our program somewhat because of the interest shown in it by various centers throughout the world. Right now we serve as a national referral center. But the implications for the program go far beyond continental boundaries. It really is a demonstration project for heart transplantation people around the world.

Who else is doing heart transplants?

Dr. Christiaan Barnard is performing them sporadically. Two other centers in the United States are interested and also perform them sporadically; one is at the Medical College of Virginia, under Dr. Richard Lower, the other is at the University of Wisconsin under Dr. Donald Kahn. There is also a center in Toronto, and there are two hospitals in Paris, where the procedure is peformed sporadically.

What are the longest survivals?

In our program the longest surviving patient is now six years and four months after heart transplantation. There are four other patients in the world who have achieved longer survivals—I believe the longest survivor is now seven years and three months.

What are the critical survival factors?

The really central features that determine survival have been recognized since the days of experimental heart transplantation, long before the advent of the clinical procedure. They revolve around the host immune responses to the cardiac graft, requiring indefinite immunosuppression. So it's in that area that the major focus of investigation is continuing. What is really needed is a way to prevent the immune response to allograft tissue in a selective, specific fashion so that we don't compromise a person's ability to mount an immune response to infection.

Have you altered your technique?

The surgical technique itself is virtually the same as it was in 1968. It had been refined in our own laboratories over the past decade, and translated into the operating room and modified slightly to adapt to the human situation. But since that time there's been no essential modification.

Have you ever considered a double-heart or "piggy-back" transplant like the one performed by Dr. Barnard?

No. The one potential advantage of the double-heart, or piggy-back transplant, is that it leaves the right ventricle in place. And the right ventricle may have chronically adapted to the elevated pulmonary pressure caused by the left heart failure. So for a patient with pulmonary hypertension, a piggy-back transplant might conceivably be useful. I don't think it's that important, though, because most of the candidates referred here and turned down for medical reasons are turned down for reasons other than pulmonary hypertension. From what I have read about Dr. Barnard, his attempts at heterotopic transplantation were really directed toward the concept of left ventricular assistance similar to that offered by a mechanical assist device.

What changes, if any, have you made in your immunosuppressive regimen?

For the past three years we've been using antithymocyte globulin, or ATG. This is a heterologous antiserum that can be raised in various species, such as rabbits, horses, and goats, that have been immunized against human thymocytes. This antiserum is purified and given early after operation as an adjunctive immunosuppressive agent in combination with prednisone and the antimetabolic agent azathioprine. In the early years of our program we were using antilymphocytic serum raised in horses. Then we changed to horse ATG. About three years ago we initiated a study of rabbit ATG. It's probably the most significant change since the beginning of the program, because since its introduction there's been an increase in the survival rate.

What are your criteria for selecting patients for heart transplantation?

Right now, basically clinical. Because we don't understand enough about immunological phenomena to be able to pick or discredit a potential recipient on the basis of his immunological function alone. The criteria are based on age, first of all—the patient has to be less than 55 years old. He cannot present with any active infection, and he cannot present with any recent pulmonary infarction or pulmonary embolism because of the tendency of these to become infected after transplantation and administration of immunosuppressive drugs. He cannot have diabetes mellitus, because that condition is worsened by cortisone. And he cannot present with severe pulmonary hypertension, but that only occurs in a minority of the patients we evaluate. A patient, obviously, cannot have a separate disease that would otherwise limit life expectancy or prevent rehabilitation. And it's important that a patient has a history of a high degree of medical compliance, and is highly motivated, because he is responsible for his own medication after discharge. Basically, the patients we take are dying of heart disease. As best we are able to determine, their life expectancy is in the range of several weeks to at most a few months. Two-thirds of the patients we take have advanced coronary artery disease with severe damage to the left ventricle so that coronary bypass by itself would not be useful. Those patients have all sustained at least one infarction, and usually multiple infarctions. The other third of the patients we take present with some obscure form of cardiomyopathy, the genesis of which is not well undestood. We see this predominantly in younger patients. In fact, the youngest patient in the series, who was 15 years old, had cardiomyopathy.

What are the prospects of heart transplantation in the near future?

Very bright. Very bright. I really do expect that in the *near* future, Stanford will remain a unique program. But as the level of success continues to rise, and I expect it will, and if any significant advances in immunology and transplantation biology are made, there'll be additional centers that will take it up—perhaps some of the very centers that dropped it in the early years of heart transplantation. Our own plans are to continue a very vigorous program and to increase its scope.

Do you think mechanical hearts will be available in the next decade or two?

I think there will be some kind of mechanical device used in the next decade. The first kinds will be assist devices, not replacements. I think these will be followed by mechanical heart replacement without internal power sources, so that the patient will still be dependent upon external sources. By the time a truly totally implantable heart is developed, clinically tested, and evaluated as successful, I think there will be patients walking around with heart transplants that have been in place 10 to 15 years.

Have you had to reoperate?

We've operated on 100 patients, and we've retransplanted two patients because of failure of the first graft. They are both living now. An additional three patients were retransplanted unsuccessfully.

Is there trouble getting donor hearts?

Intermittently, there are problems with the supply of donor organs. It's really one of the most important parts of the program, I think, in terms of public education about the need for organs for transplantation. Not just the heart; the kidneys, tissues of all kinds including skin, corneas, earbones, skull bones, cartilage and so forth. I see this as a societal problem in terms of education and public awareness.

(The other members of the Stanford team, in addition to Drs. Shumway and Stinson, are cardiovascular surgeons Randall Griepp and Philip Oyer; immunopathologist Charles Bieber; pathologist Margaret Billingham; social worker Lois Christopherson; cardiologists John Schroeder, Jay Mason, and Sharon Hunt; immunologists Alan Coulson and Lyle David; surgery resident Bruce Reitz; and cardiology fellows Don Ricci, Art Orlick, Dale Stemple, and Steve Pope.)

Dr. Edward B. Stinson, the member of Stanford's heart transplant team who answered the questions on this page, is shown (right) operating with Dr. Norman Shumway, the principal investigator for the transplant program.

Cell 'Clone,' Not Cholesterol Buildup, Seen in Atherosclerosis

By JOHN HENAHAN
Special Tribune Correspondent

ANAHEIM, CALIF.—The theory that atherosclerosis is the result of a tumor-like proliferation of a single cell "clone" rather than a simple buildup of cholesterol in the arteries received new support at a symposium of the 60th annual meeting of the Federation of American Societies for Experimental Biology held here.

As first proposed about three years ago by Dr. Earl P. Benditt, of the University of Washington, Seattle, the idea suggests that cell proliferation is first initiated by some chemical, biological or physical stimulus and that the growing mass is then built up into an atherosclerotic plaque as it is invaded by fibrinogen, lipoproteins and other blood components. The theory was based on his observations that atherosclerotic plaques from the aortas of three women all contained only a single form of two possible forms of the enzyme glucose-6-phosphate dehydrogenase, indicating that the atherosclerotic tissue must have come from only one cell population, Dr. Benditt, chairman of the FASEB symposium, said.

Confirmed at Hopkins

His work has since been confirmed by Dr. Robert H. Heptinstall, of the Johns Hopkins University School of Medicine, who told a press conference that Dr. Benditt's finding is "one of the most significant observations that has been made in the entire field of arteriosclerosis over the last 20 years. In fact, it took something like this to get me back into the field."

It is still not clear what factors act upon a cell or family of cells to initiate the atherosclerotic process, said Dr. Benditt, but he suspects that chemical mutagens from the environment, or perhaps viruses such as those that cause warts could be implicated. Presumably these initiators are carried to smooth muscle cells in the arterial walls by blood components, such as lipoproteins, he said.

For example, he reported laboratory evidence that 3-methyl cholanthrene, a pre-carcinogenic mutagen found in cigarette smoke and lipoproteins from human serum are carried in the same portion of the serum as is cholesterol.

"It has now been observed in several laboratories that low density lipoproteins, among the serum proteins, are preferentially taken up by the smooth muscle cells derived from human and primate artery walls when cultivated in vitro," Dr. Benditt said.

Evidence Forthcoming

"In addition, evidence is beginning to appear that there is an enzyme system—aryl hydrocarbon hydroxylase—that converts substances such as 3-methyl cholanthrene from a pre-mutagen to a mutagen. Thus we begin to see that several of the ingredients required for initiation of monoclonal growth in artery wall cells are present in the human system. . . . We can now sketch the outlines of how one risk factor, cigarette smoking, may be operating to produce or to enhance the occurrence of atherosclerotic lesions."

Whatever initiates atherosclerotic cell proliferation first passes into the blood stream via the gastrointestinal tract, lungs or skin, Dr. Benditt proposed. "The inner lining of the vessels," he added, "thus become exposed to injurious environmental agents, and being a specialized, but otherwise ordinary tissue, it responds by producing inflammatory responses to infections, and by tumor formation with the appropriate stimuli."

Another initiator for atherosclerosis could be cholesterol-α-oxide, a known tumor-inducer which has also been found in substantial concentrations in the serums of people prone to atherosclerosis, including those with Type II hypercholesteremia and hypertension, he said. In addition, animal studies in Dr. Benditt's laboratories indicate that hypertension, even of brief duration, "causes increased multiplication of the endothelial lining cells of arteries."

The possibility that viruses—especially in combination with estrogenic hormones—may also act as initiators came from Dr. Benditt's findings that chickens which develop atherosclerosis spontaneously developed a much more advanced case of the disease if they were simultaneously injected with estrogens and afflicted by a virus.

"This observation seems specially important when we recall that in [a] recently completed coronary drug project, the administration of estrogens was associated *not* with a decrease, but with an *increased* death rate from myocardial infarction . . . The effects of estrogens in eliciting latent viruses and inducing lymphomas in mice have now been observed. Could this be the mechanism involved in the estrogen portion of the coronary drug project?" Dr. Benditt asked.

In addition, he said, the fact that several young women with lupus erythematosus (presumably viral in origin) died of thrombosis due to atherosclerosis suggests that "we may have our first virus cause of atherosclerosis."

Dr. Heptinstall presented findings which strengthen Dr. Benditt's theory that atherosclerosis is the tumorous (albeit benign) end product of the proliferation of a single cell clone. Using the enzyme marker glucose-6-phosphate dehydrogenase, he confirmed that the "yellow fatty streak" in arteries, which is considered by many to be the forerunner of a mature atherosclerotic plaque, shares the same enzyme pattern. The streaks, found in the arteries of human juveniles, consist of groups of fat-filled cells, he explained, concluding that his data are "consistent with the notion that some streaks act as the forerunner of the fibrous plaque."

Nursing Home Loans

HARRISBURG, PA.—Pennsylvania state's Nursing Home Loan Agency has amended its regulations to allow institutions providing nursing care to apply for long-term, low-cost loans. Pennsylvania is the first state to do so.

Renography Urged in Dx of High BP Secondary to Renovascular Disease

Medical Tribune Report

DALLAS—Renography is the best tool presently available for screening patients for hypertension secondary to renovascular disease, according to Dr. M. D. Blaufox, of Albert Einstein College of Medicine.

"There are about 20 million persons with hypertension and about 5% of these are potentially curable," he said. "Yet there is not one single symptom that will tell a physician whether the patient's hypertension is caused by renovascular disease."

"We need an accurate, safe and inexpensive screening test," Dr. Blaufox told the Society of Nuclear Medicine meeting here.

While admitting there is no procedure capable of detecting renovascular hypertension with 100% accuracy, Dr. Blaufox said the renogram was the most accurte, safest and least expensive procedure available.

Dr. Blaufox said comparative studies have shown that renograms can diagnose renovascular hypertension with about 85% accuracy adding, however, that they also have a false positive rate of about 10%. By contrast, urograms show about a 78% accurate detection with 11% false positives.

When both tests are done, renovascularly induced hypertension can be detected accurately 91% of the time, he said. By the same token, however, the false positive rate increases to 18%.

While the two procedures are comparable in accuracy, Dr. Blaufox stated, about 6% of the patients experience reactions to the contrast medium used in he urograms while there were "virtually no reactions to the renograms."

Renography should only be used for screening renovascular hypertension in highly selected cases, the investigator cautioned.

helping your patients

This MEDICAL TRIBUNE *feature is intended to help the physician find things his patients may need. It is based on data from the* Self-Help Manual for Arthritis Patients, *prepared by Judith Lannefeld Klinger, O.T.R., M.A., for the Allied Health Professions Section of the Arthritis Foundation, 745 Riverside Drive, New York, N.Y. 10027.*

In the Bathroom

The *Manual* offers several suggestions that may help persons with arthritis of the lower extremities to manage toilet activities independently. For example, a raised toilet seat, in a permanent or portable model, greatly reduces stress on hip and knee joints. Armrests can be attached to seat bolts. A safety bar fixed to the wall would help in transfering from wheelchair to toilet. In remodeling a bathroom, hanging a wall toilet higher than usual, or installing a special 18-inch high bowl, are possible solutions.

When self-cleaning is difficult, the suggestion is to fashion a toilet paper holder from a metal knitting needle by bending it into two overlapping circles, like a paperclip. The clip is then set in a lightweight nonslip handle. Also, 16-inch tongs for gripping toilet paper can be purchased for about $6.

A simple homemade device, fashioned from a funnel and hose, can be used when urinating from a wheelchair; its commercial equivalent sells for about$3 to $5.

These and other personal hygiene items can be purchased from hospital supply or self-help equipment firms listed in the *Manual*, available from the Arthritis Foundation for $1.25.

Raised toilet seat reduces stress on hip and knee joints by adding 3 to 5 inches to height. Cushioned model above sells for about $32; uncushioned about $24.

Glider-commode chair can be used either with a pan or rolled over a standard toilet. Costs about $98.

Armrests divide stress between upper and lower extremities, provide balance while sitting. Cost range: $15-$25.

Tested by time and experience in the treatment of MBD

1962

"...a considerable decrease of hyperactivity...."[1]
Knobel, 1962

Over a decade of controlled studies and clinical experience has shown the effectiveness of Ritalin in reducing the hyperactivity,[1-3] distractibility,[1,4,5] and disorganized behavior[1-8] in the MBD child.

By lessening the effects of motor and attentional disorders, Ritalin can help the MBD child to better focus his attention on meaningful stimuli and thus can often improve cognition and promote learning.[8,9]

And side effects – insomnia and appetite loss – with Ritalin have occurred less frequently than with dextroamphetamine.[10,11]

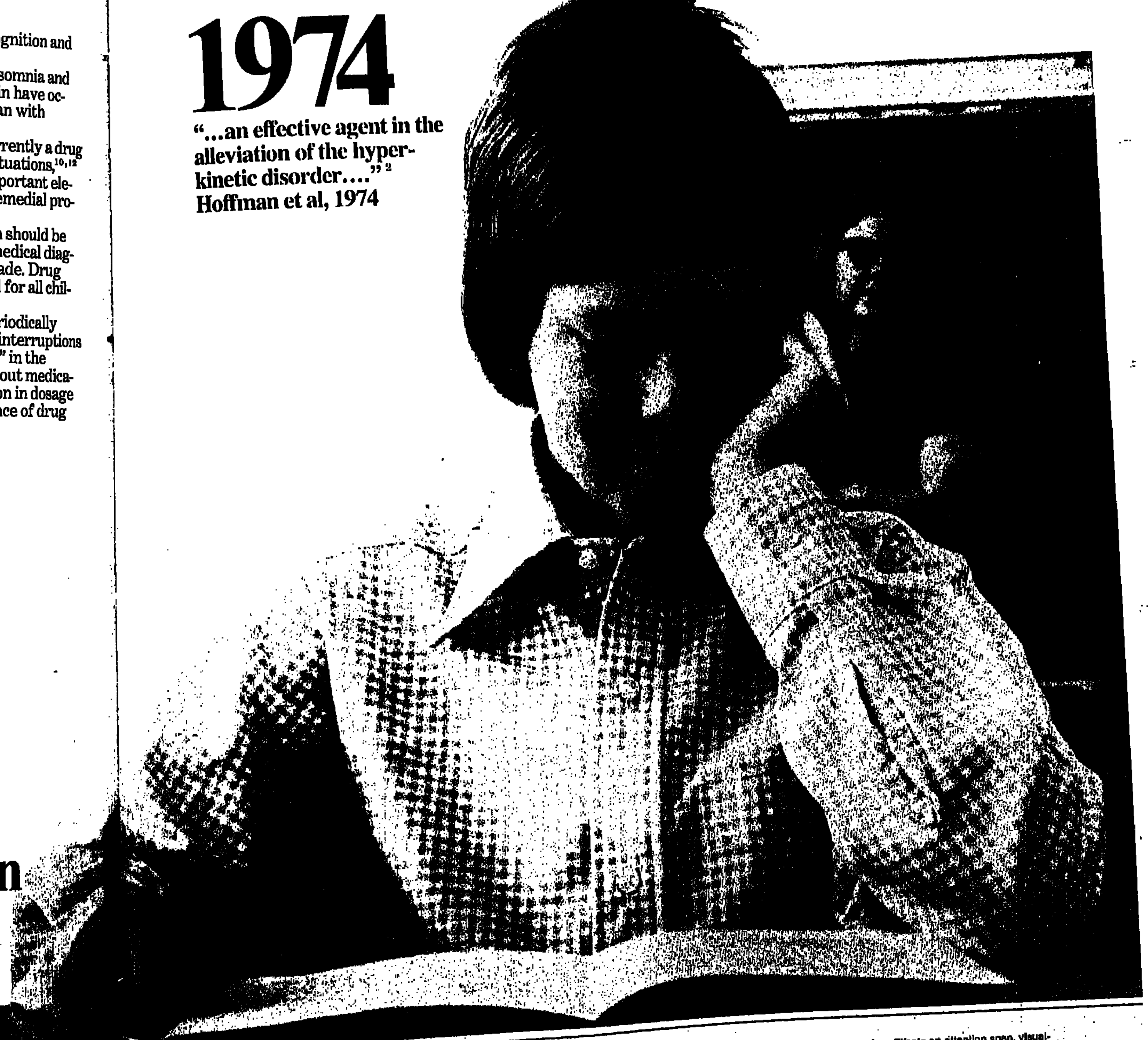
Indeed, Ritalin is currently a drug of choice in many MBD situations,[10,12] and can prove to be an important element in many complete remedial programs for MBD.

Therapy with Ritalin should be undertaken only after a medical diagnosis of MBD has been made. Drug treatment is not indicated for all children with MBD.

Dosage should be periodically interrupted. Often, these interruptions reveal some "stabilization" in the child's behavior even without medication, permitting a reduction in dosage and eventual discontinuance of drug therapy.

1974

"...an effective agent in the alleviation of the hyperkinetic disorder...."[2]
Hoffman et al, 1974



Ritalin®
(methylphenidate)
Only when medication is indicated

References:

1. Knobel M: Psychopharmacology for the hyperkinetic child. *Arch Gen Psychiatry* 6:198-202, 1962. 2. Hoffman SP, Engelhardt DM, Margolis RA, et al: Response to methylphenidate in low socio economic hyperactive children. *Arch Gen Psychiatry* 30:354-359, 1974. 3. Sprague RL, Barnes KR, Werry JS: Methylphenidate and thioridazine: Learning, reaction time, activity, and classroom behavior in disturbed children. *Am J Orthopsychiatry* 40:615-628, 1970. 4. Knights RM, Hinton GG: The effects of methylphenidate (Ritalin) on the motor skills and behavior of children with learning problems. *J Nerv Ment Dis* 148:643-653, 1969. 5. Seger EY, Hallum G: Methylphenidate in children with minimal brain dysfunction: Effects on attention span, visual-motor skills, and behavior. *Curr Ther Res* 16:635-641, 1974. 6. Conners CK, Eisenberg L: The effects of methylphenidate on symptomatology and learning in disturbed children. *Am J Psychiatry* 120:458-464, 1963. 7. Creager RO, Van Riper C: The effect of methylphenidate on the verbal productivity of children with cerebral dysfunction. *J Speech Hear Res* 10:623-628, 1967. 8. Comly HH: Cerebral stimulants for children with learning disorders. *J Learning Disabil* 4:484-490, 1971. 9. Mackay MC, Beck L, Taylor R: Methylphenidate for adolescents with minimal brain dysfunction. *NY State J Med* 73:550-554, 1973. 10. Paine RS: Syndromes of "minimal cerebral damage." *Pediatr Clin North Am* 15:779-800, 1968. 11. Conners CK: Symposium: Behavior modification by drugs: II. Psychological effects of stimulant drugs in children with minimal brain dysfunction. *Pediatrics* 49:702-708, 1972. 12. Charlton MH: Symposium: Minimal brain dysfunction and the hyperkinetic child: Clinical aspects. *NY State J Med* 16:2058-2060, 1972.

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Text of Interview: Part II

Dr. Cooper: Old Data + New Trials Assure No Chronic Toxicity in Swine Flu Vaccine

Above, Dr. Cooper testifies before House health subcommittee. In interview text on this page he points out: "The incidence of febrile reactions to the swine flu vaccine [in field trials in 5,000 people] . . . was 1.2% and was not significantly different from that seen in participants who received placebo."

What acute toxicity data is available on the swine flu vaccine presently being produced?

Influenza viruses, and subsequently vaccines against them, have been subjected to acute toxicity tests in a number of animal models since the 1930's. The properties of the vaccines are well known and a matter of scientific record. We also have the experience of past clinical trials with influenza vaccines from which to draw. As the Public Health Service Advisory Committee on Immunization Practices said recently, "influenza vaccines currently produced by manufacturers in the United States are purified by zonal centrifugation and should produce a few severe side effects . . ." Nevertheless, the present vaccine against A/New Jersey/76 was first subjected to routine animal tests to determine that nothing untoward would happen.

In effect, isn't it true that we do not have available the same type of acute toxicity data for this vaccine as is required for drugs? Vaccines have been associated with hazard and have been a serious subject of debate in Britain, have they not?

We have 30 years of experience with influenza vaccines in use. In addition, in recently completed trials more than 5,000 persons received the influenza vaccines that will be used in the national immunization program. Individuals receiving the vaccine have had detailed clinical observation during the period when it would be expected that vaccine-associated reactions would occur. These tests showed that, overall, the incidence of febrile reactions to the swine flu vaccine, in the dosage range which will be used in the immunization program, was 1.2% and was not significantly different from that seen in participants who received placebo. The incidence of such reactions in older people receiving the bivalent vaccines was at a maximum 2%. Constitutional symptoms following inoculation were also similar in incidence in vaccine and placebo recipients—about 5 to 6%.

Vaccines and use of vaccines have always been the subject of debate in this country and elsewhere. It is worth noting however that the British are planning to immunize their high risk influenza group this year and intend to include the swine virus in the vaccine they will be using.

Do you believe that the Advisory Committee's observation that "only mild local reactions such as erythema and tenderness at the injection site, will be relatively common" excludes the possibility of more serious complications as have occurred with other vaccines?

In general, yes. The only major exception here would be possible severe reactions in persons with egg allergies. There have simply not been other kinds of reactions other than those normally associated with flu vaccines reported in the literature over the years. Of course, you can't ever rule out the idiosyncratic occurrence in medicine.

It has been reported that at least six countries—Germany, Switzerland, Denmark, Hungary, Japan and even Monaco—provide compensation for children who have been damaged by vaccines but is it not a fact that our law exempts the government from liability in the event of an individual's sustaining damage from the swine flu vaccine program?

Compensation for damages has always been available through the courts in this country, and the liability issue is a serious one here. We have just introduced legislation in the Congress which would allow us to indemnify the manufacturers from claims arising from the inoculation with the vaccine. It would not cover claims arising from negligence on the manufacturer's part, however. The effect here is for the government to assume liability for events that may occur in areas of its responsibility; we have said that we will be responsible for the testing of the vaccine to assure safety and effectiveness, and for adequately informing recipients of the vaccine of its benefits and risks.

Would you favor our government affording economic, "insurance"-type coverage for vaccine-damaged children if:

(a) vaccination is compulsory as it used to be for smallpox, or

(b) vaccination is voluntary but recommended by the government?

Compensation for unexpected damages arising from administration of any medicine unrelated to negligence ought to be available. But whether it is the government that ought to provide that liability coverage directly is a matter for debate and is, in fact, an issue which we have been considering here for over a year. At present we do not have a position on it.

Does not the decision for the vaccination program bypass the chronic toxicity data required for drugs?

The same body of data covering past experience in using influenza vaccines and our vast knowledge of the behavior of the virus during natural pandemics provide adequate assurance that there is no chronic toxicity problem involved with this vaccine.

In contrast, drugs usually contain ingredients which are completely foreign to the body, either as naturally occurring contaminants or as part of pharmaceuticals. Long-term toxicity studies are more likely to be required for these agents because our in vitro data is far more limited, if not nonexistent, and the drugs themselves are more apt to be used on a long-term basis, whereas vaccines are not administered repetitively over long periods.

Drugs must be studied for carcinogenicity and teratogenicity. Has this not been bypassed in respect to the swine flu vaccine?

Again, we can draw upon the scientific literature for information about potential carcinogenicity or even teratogenicity of influenza virus or vaccines. These studies have produced no evidence of a problem, nor is there evidence of increased cancer or birth defects as a result of influenza pandemics.

In the next issue, the HEW official discusses with Dr. Sackler the use of prisoners in clinical trials, the efficacy of the vaccine and certain philosophical aspects of the nationwide vaccination program.

Test for Amylase in Sputum Confirms Gastric Aspiration

By ANASTASIA TOUFEXIS
Medical Tribune Staff

NEW ORLEANS—A relatively simple new way to document aspiration of oral or gastric contents by measuring amylase activity in sputum was described here at a meeting of the American Lung Association.

"Sputum amylase is a reliable way of detecting contamination of the trachea with saliva if performed within eight hours of aspiration," reported Dr. Dorsett D. Smith, director of the chest clinic and Assistant Professor of Medicine at the University of Washington in Seattle.

Aspiration is a common respiratory problem that is often difficult to diagnose, the investigator noted. The only conclusive proof heretofore, he said, has been the demonstration of oral or gastric contents in the airways using fine-fluoroscopy, methylene blue, or the actual finding of aspirants in the lung at the time of intubation.

"Many clinical situations occur where pulmonary infiltrates are present," he added, "but other diagnoses, such as fat embolism, lung confusion, bacterial pneumonia, or adult respiratory distress syndrome cannot be excluded. Other patients have recurrent bouts of lower lobe pneumonia, where aspiration is suspected but cannot be proved."

Dr. Smith and Dr. Thomas McNamara, chief of the clinical laboratory at Providence Hospital in Everett, Washington, studied 70 patients in intensive or coronary care units, all of whom were either intubated or had a tracheostomy tube.

Amylase activity in sputum was determined for a control group with no evidence of aspiration, a second group in whom aspiration was suspected clinically but not confirmed, and a third group of patients with documented aspiration.

The mean value for the control group was 341 units/ml, for the suspect group 2,764, and for the aspiration group 63,217, according to the report. Normal tracheal amylase is 0 to 1,000, compared with 9,000-150,000 for salivary amylase and 0-60,000 for gastric amylase, Dr. Smith said, and thus elevated tracheal amylase values indicate probable aspiration.

"Documenting aspiration is obviously not a major problem when the patient is in acute distress," Dr. McNamara told MEDICAL TRIBUNE. "The problem comes up when the diagnosis is not so obvious.

"You have a patient who is evidently experiencing some respiratory difficulty. The question then is 'Did this patient aspirate earlier in the day when not under direct observation?' " Nursing home patients in particular fall into this category, he noted.

"This test is easily done and can provide the clinician with reassurance that the diagnosis of aspiration is correct," he said.

Both doctors stressed that the test must be performed within 8 hours of suspected aspiration. After that time, amylase activity falls rapidly and test values are not appreciably elevated.

Insect Allergy

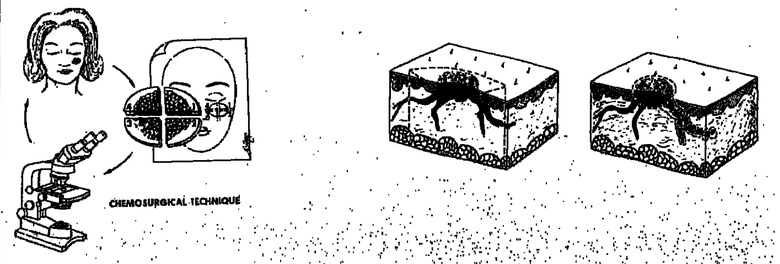
Medical Tribune Report

HOLLYWOOD, FLA.—One of the highlights of the combined meeting of the Pan American Medical and the Florida Allergy Associations, to be held here Oct. 24-29, will be a half-day symposium (Oct. 26, 2-5 p.m.) on insect allergy conducted by Dr. Claude A. Frazier, of Asheville, N.C.

Six allergy specialists will speak on such subjects as: allergic reactions to insect stings and bites, in vitro diagnosis of insect allergens, immunology and toxicology of venoms, and hyposensitization.

Dr. Frazer recently contributed an "In Consultation" article on insect allergy to MEDICAL TRIBUNE (July 7, 21).

Cleveland Clinic Now Offers Mohs Chemosurgery



Step-by-step diagram of tumor removal using Mohs chemosurgery is represented above. Excised layer of tissue is examined microscopically to form a "map" of the tumor, at far left. Malignancy is traced in quadrants, preserving normal tissue. Cutaway shows how conventional surgery, middle, removes more healthy tissue than chemosurgery, right. The layer-by-layer technique is now used in the new Section of Chemosurgery at Cleveland Clinic.

Tribune Economic Analysis

Indicators of Market Strength –And Weakness

BY ELIOT JANEWAY
Consulting Economist

The popular indicator of stock market strength is the Dow Jones Industrial Average; and most eyes follow its ups and downs, even when it is not hovering at the symbolic 1,000 level: holding just a shade above symbolizes general market strength; falling back signals weakness.

Analysts have four other tests. The first two—the volume of trading and the breadth of advances–examine the performance of the market as a whole. The second two—the action of the transports and the utilities—confirm the leads given by the Industrial Average. All four indicators have been positive during these recent weeks of Industrial Average listlessness.

The parameters of market strength and weakness were set earlier in this decade. The minimum trading volume for sustaining price strength is 30 million shares a day. At the opposite extreme, 15 million shares a day is the borderline of disaster.

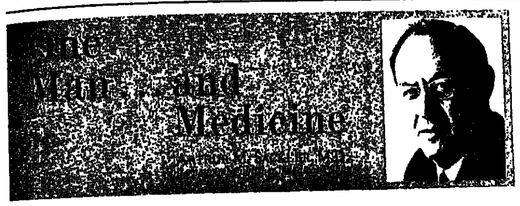
The recent volume recovery toward 20 million shares points to a bullish resolution of the stalemate.

Ask Janeway

Please comment on my own idea of a retirement fund or fund available in case of illness. My wife and I first purchased U.S. "E" bonds in 1971 $10,000 also in 1972, 1973, 1974, and $20,000 in 1975. At my age of 72, we are on Social Security, and I am fully employed. In case of my illness or forced retirement I figure that I could have $10,000 available this year in $1,000 amounts monthly or whenever needed, thus avoiding income tax on a $10,000 amount at one time. Where would transfer to "H" bonds come into the picture? Could they be purchased in amounts allowed in addition to "E" bonds yearly? How might the "and/or" investment affect estate taxes? Pensylvania Internist

You settled for less than a market in buying "E" bonds; you would do this again in buying "H" bonds. If you want to anticipate state tax at a discount, buy "flower" bonds. You will find them described in my handbook, *You And Your Money.* They are available at discounts during an investor's lifetime and are usable at death to settle estate tax at par. The way this works, if you buy a "flower" bond for $900, your estate may turn it in to the Treasury for redemption, and claim $1,000 worth of credit.

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, *880 Third Avenue, New York, N.Y. 10022.*



What Does a Patient Really Want?

I'VE JUST BEEN THROUGH my "annual" physical. It was reassuring—and demonstrated once again, as has been reported in the literature, the role of a good balance scale in identifying the commonest change found in routine check-ups. But above all, it bore home to me, as "patient," the importance of the understanding and tenderness, the thoughtfulness and humanity of my doctor. It couldn't help but loose a flood of associations and observations on the changing medical scene.

Of late we have heard much of what's wrong with doctors, so little of what's good. The criticism, it seems, depends on who the critic is.

What Do the Mass Media Want?

Some newspapers rake for muck in the physician-patient relationship and produce headlines to feed sensationalism and subscriptions. Even the best of papers run stories which tell not of the 80% to 90% confirmable medical decisions for surgery, but focus on a small percentage which they then mislabel "unnecessary surgery," extrapolate irresponsibly, and trumpet that thousands of patients are "killed"—"Do You Trust Your Doctor?"

What Do Government Officials Want?

Many government officials view the problems in physician-patient relationships from the standard perspective of a bureaucracy. If a problem exists, and even sometimes when it doesn't, all will be well if you pass a few laws, add some regulations and of course increase the manpower of the staff so that "they" will set it all right again. How? After setting more standards and more certification, add recertifications; change from optional to mandatory requirements and, of course, make all doctors accountable to "them."

What Do Consumerists Want?

The public crusaders join in the hue and cry:

"Doctors don't know what they are doing." We need more government control of research; the government is not trustworthy. At one time we had "too few hospital beds", now "we have too many." We have "too few" primary physicians; we have "too many" surgeons and specialists. Medicines are "killer drugs", the disadvantaged shouldn't be denied the benefits of modern medicines.

Government agencies are venal and serve vested interests; let's get more laws and more regulations to give more power to these agencies. We need more and more double-blind tests for anticancer drugs and for effective cardiovascular agents; let's adopt new systems of national health care without pilot plans or prototypes, without any tests—blind or double-blind.

Why?

What Does The Patient Want?

And the patient? The patient wants a physician he can believe in and trust; a physician who can relieve his pain and calm his anxiety; a physician who reassures him when he is well and gives him hope when he is ill.

And what does the patient think? He thinks that the medical profession is the most deserving of his confidence and faith; more so than politicians and bureaucrats who seek to control medicine and the men of medicine; more than the publicists and the press that derogate doctors. Yes, even more than the ministry. For the public believes, as do most physicians, that medicine is still a calling.

* * *

As I travel around the world, I am fascinated by certain common attributes of those who are called doctor, those who see themselves as healers of the sick—physicians. Despite the difference in language—English, French, or German; Polish or Portugese; Russian or Chinese—physicians share a common goal, *to keep people well and to relieve pain and suffering;* and they have in common a pride in our profession. Common goals and identification override not only language but political structure and economics as well. They give the lie to those who hold that physicians are physicians primarily or solely for economic advantage because in country after country being a physician entails sacrifice of fiscal rewards as well as of self.

Do physicians fail? On occasions, without doubt; with the best of intentions "man" is fallible. Infallibility is reserved for few. Mankind in its wisdom recognizes the rarity of infallibility by attributing this quality to those it worships as gods.

EPIGRAMS—Clinical and Otherwise

In everything that relates to science, I am a whole Encyclopedia behind the rest of the world.

Charles Lamb
(1775-1834)
Essays of Elia, "The Old and the New Schoolmaster"

Medicine on Stamps

Saint Vitus

St. Vitus (circa 283-301) was the only son of a Roman Senator in Sicily. At about age 10, he became a Christian without the knowledge of his parents. His father tried to change his mind by torture and threats, but he escaped to Lucania. Later he went to Rome where he miraculously cured the son of Emperor Diocletian of fits, only to be accused of witchcraft and tortured to death. Since then he has been identified with chorea, a convulsive nervous disorder with irregular movements: "St. Vitus Dance."

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Arterial O_2 Test Advisable in Sarcoidosis

Medical Tribune Report

PHILADELPHIA—If sarcoidosis patients don't seem to respond to steroid therapy, a major reason may be that the usual methods for measuring response are too insensitive to do the job.

That conclusion was offered here by a Cleveland team who reported that a controlled trial of high-dose corticosteroids had demonstrated improved pulmonary gas exchange in patients with sarcoidosis, when alveolar-arterial oxygen differences were measured, but not when more usual assays were done.

Challenging the inconclusive or contradictory results of steroid therapy reported by some other investigators, the team said the drawbacks of such tests as physiologic measurements of lung mechanics and of diffusing capacities are that they demonstrate characteristic abnormalities that correlate with the disease in the presence of severe structural damage. But these tests may fail to correlate with marked clinical and radiographic changes.

20 Patients Treated

The findings were described at the annual meeting of the American College of Physicians by Drs. Gerald M. Fleming, Hugo D. Montenegro and Edward H. Chester of Case Western Reserve University.

Their study series included 32 patients with sarcoidosis and other diffuse interstitial lung disease. The treated group of 20 patients included 12 with sarcoidosis; in the 16 controls, there were nine with sarcoidosis. Mean ages of the treated and untreated patients were similar. Several patients had been referred to the team, the investigators said, because of a recent deterioration in their clinical status, suggesting an active inflammatory phase of the disease. These included 13 of the 20 in the treatment group and 10 of the 16 untreated patients. Symptoms predominantly included increasing dyspnea, cough, weight loss, malaise and sputum production.

Prednisone Given

The treated patients received a trial of prednisone, 30 to 60 mg daily, and the studies were repeated at the average interval of three months.

"There was a significant deterioration with time in the untreated patients for both total lung capacity and vital capacity. There was an apparent, but not significant, improvement in these parameters with steroids... The diffusing capacity was abnormal in both groups, but no significant change was observed at followup."

However, the steroid-treated patients demonstrated "a significant improvement in gas exchange at follow-up measured by alveolar-arterial oxygen differences, at all three levels of oxygenation—14%, 21% and 100% inspired oxygen and room air during exercise, but not by steady-state diffusing capacity," the team reported. "There was no change in pulmonary mechanics except for a small increase in vital capacity."

In the untreated patients, alveolar-arterial O_2 gradients remained unchanged with all four methods.

"In conclusion," the group commented, "we have demonstrated that corticosteroids can improve pulmonary gas exchange significantly in patients with diffuse interstitial lung disease, including patients with chronic disease. In addition, we have shown that tests of ventilatory mechanics and of diffusing capacities, although frequently abnormal in these conditions, are insensitive methods for longitudinal monitoring of the course of the disease... Therefore, we recommend that patients with diffuse interstitial lung disease, including chronic disease, receive a trial of high-dose corticosteroids. Gas exchange should be assessed by gradients or by rest and exercise blood gases before and during the therapeutic trial. Patients who have not responded should be weaned. For those who have improved, gas transport studies can be used as a management tool to guide continuing therapy."

Skin Cells Cultured

Medical Tribune Report

CAMBRIDGE, MASS.—Human skin cells—previously resistant to attempts to grow them in the laboratory—can now be easily cultivated, using a technique developed by biologists here at the Massachusetts Institute of Technology.

The biologists, Professor Howard Green and former graduate student James G. Rheinwald (now a postdoctoral fellow) say that the technique could be useful both in basic research and in medical research.

For example, skin cells grown in the laboratory could be used to study the effects of viruses such as the wart virus, to study the behavior of skin cells involved in diseases, and to test drugs.

It may also be possible to grow large quantities of a patient's skin to be used in skin grafts.

from Japan

New Hog Valve Implanted in 40 Heart Patients

Continued from page 2

on 26 cases of cardiac sudden death. According to him, responsible etiologies included diminutive narrowing of the whole coronary bed, selective constriction of the A-V node artery, and anomaly in the stimulation conduction system. The investigator further pointed out that the etiology first mentioned was responsible for senile deaths, and the A-V constriction caused deaths among youths and the midaged, while the conduction disorder was responsible for infantile deaths.

from France

Clinicians Define Chronic Form Of Bronchitis

Continued from page 2

superinfection, particularly in younger patients. Dr. Ledu stressed the importance of functional respiratory examinations, especially after repeated infections, saying that this served as the basis of his diagnosis.

Prof. Catllina reported that his industrial medicine department examines 125,000 subjects annually, focusing on job fitness, not health. However, their study also includes working conditions and is completed by fluoroscope. He said that although industrial doctors do not deal with repeated acute episodes of bronchitis, which often mark the starting point of the chronic affection and are treated by general practitioners, both types of physicians are in the same situation in diagnosing chronic bronchitis. Elaborate diagnostic equipment is not necessary in tracking down the disease, he remarked. The use of various pulmonary function test apparatus generally reinforces and confirms the standard clinical examination.

There are no determining industrial circumstances contributing to chronic bronchitis, Prof. Catilina said, except perhaps open air work with bad weather exposure or work in cold storage industries.

from Britain

'Vacuum Cleaner' Removes 100% of OR's Waste Gas

Continued from page 2

ish Medical Association's Annual Film Competition seems most appropriate.

The film "Extraction of Anaesthetic Gases from Operating Theatres" was made by Dr. P. Cliffe, of the Department of Clinical Measurement, and Dr. P. Hansell and Mr. K. P. Dugnid, of the Department of Medical Photography and Illustration, Westminster Medical School, London.

The making of the film stemmed from a 1974 U.S. report on the risks of working in operating theatres. This report was the first to indicate that women working in operating theatres were at risk of spontaneous abortion and of having babies with congenital abnormalities, while male staff had an increased risk of hepatic disease.

The Westminster group's approach to the problem was to try and visualize the flow patterns of different gases from the expiratory valve of the anaesthetic mask. The next step was to assess how the waste gases could be removed.

A "vacuum cleaner" arrangement was rigged up. It consisted of a compact hood not attached to the mask but placed close over it. The hood was then connected to an extractor pump.

The team found that with this system installed, waste gases can be scavenged with 100% efficiency.

from Germany

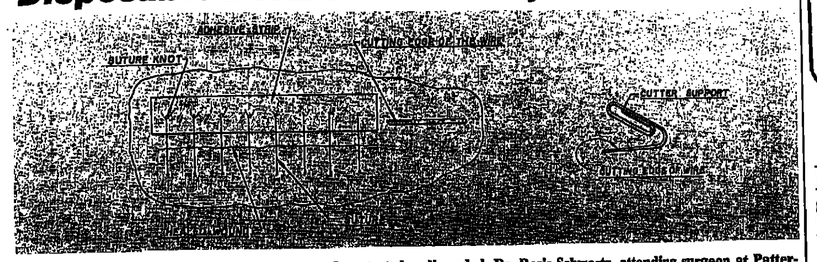
Smokers Found At High Risk of Bladder Cancer

Continued from page 2

the investigation, 213 had already died. The surviving 1585, of whom 51.1% had papilloma and 48.9% carcinoma were interrogated in writing, and replies of practical value came from 500 persons (400 men, and 100 women) of whom almost two-thirds had had a vesical papilloma and the remainder carcinoma.

Most of the patients were over 60 years old. Seventy percent had started smoking before the age of 19; the corresponding proportion for the total population is 10% lower than that. No substantial distinction could be found for the incidence of the benign or malignant tumors dependent on smoking habits, nor cognate with duration of abstinence by former smokers. A striking fact was, however, that the latter had only ceased smoking a comparatively shorter time than had been expected from the control statistics; 40% had stopped during the last 10 years, and less than one-third more than 20 years before. Duration of cigarette smoking was but rarely less than 20 years, actually 30 to 60 years in most of the subjects, and from that it could be deduced that the average number of cigarettes smoked per person lay between 200,000 and 400,000. No difference was discernible between carriers of papiloma and carcinoma.

Disposable Suture Removal System Patented



Suture removal is faster and easier with a recently patented cutting device. Adhesive strip placed over knots in sutures (left) is used to lift them off skin as "paper-clip" cutter (right) is slid underneath, cutting each suture. Tape is lifted from skin, pulling the cut sutures with it, and cutter and tape are discarded. Dr. Boris Schwartz, attending surgeon at Patterson General Hospital, N.J., and the system's inventor, notes that other disposable instruments "are usually ineffective because the forceps seldom grip and the bulky scissors put pressure on what may be a tender wound."

wine talk

By JOHN CHAMBERS
Author and Consultant to Morrell & Company, New York Wine Merchants

The Current Wine Market

FOR THE PAST two years wine prices have been dropping steadily, but all good things come to an end, and prices should begin climbing again within a year's time. This alone would make the next six months a good time to buy, but there is another factor. The 1975 vintage in Bordeaux and in Germany is superb, and the opening prices are considerably lower than they will be later when scarcity begins to set in. Here is a quick survey of recent vintages in the major wine-producing areas.

Bordeaux: The '75 vintage is very fine, and the current "futures" prices (wine bought now for later delivery) are reasonable because the growers need quick money to finance the glut of light '72 and '74 wines and the light but somewhat better '73s. As these stocks clear, '75 prices will go up. '70, '71, '67, and '66 are good vintages if priced low enough. '70 and '71 are the vintages to look for in white Bordeaux, and when they become available, the '75s.

'69, '71 Superb

Burgundy: The '69 and '71 vintages are superb, and the '70 very good. '72 also is very good, but requires choosing. '73 red Burgundies are lighter and will be ready to drink before the '72s. Since the vintage was large, prices should be quite reasonable. '74 Burgundies were not particularly successful, and the '75s are worse. In Beaujolais look for the '73 and '74 vintages. The '75s are less good and will be more expensive. Indeed, if you want Beaujolais to drink over the next year, buy it as soon as possible. '73 is the white Burgundy vintage to look for, but the '69s and '70s were very fine and will last for several years to come. The light but elegant '74s are good also.

Germany: The '75 vintage is superb, particularly in the Moselle. The '69s except for the *auslesen* are showing their age, but the '71s are beautiful although hard to find and expensive. The '73s are good wines, particularly at the kabinett level, and prices on the vintage are good. However, buy the '75s now for future delivery; the prices are still reasonable and the vintage very fine.

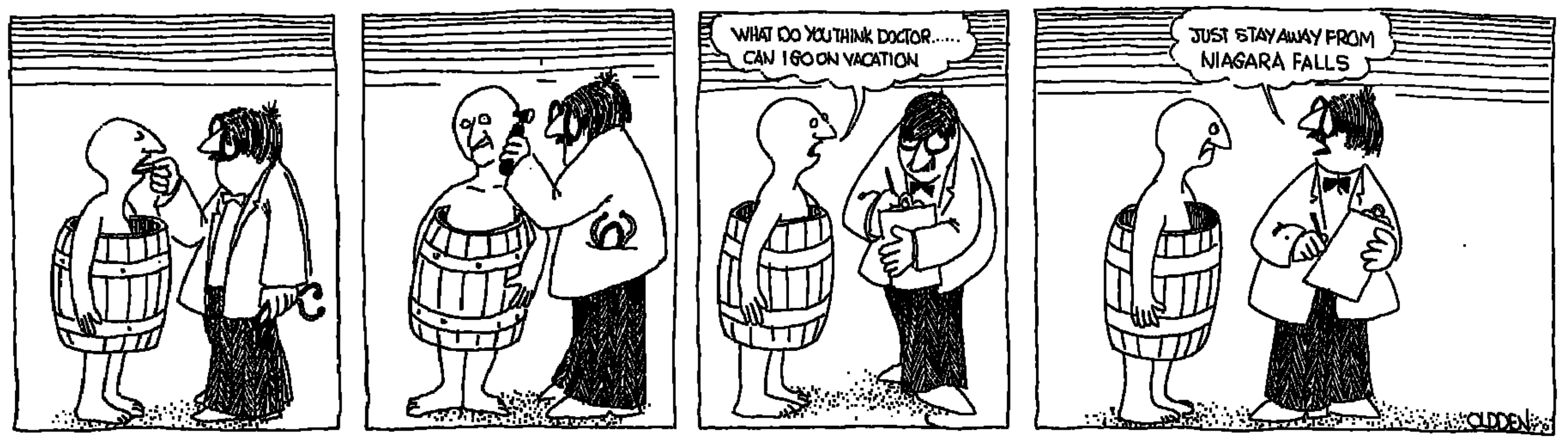
Elsewhere: '73 and '71 are tops for both the Loire and Alsace, '69, '70, and '71 for Champagne, and '70 and '71 for the Rhone. In port buy the '60 and '63, and when they come in, the '66, '67, and '70. The best recent Italian vintages are '58, '61, '64, '67, '70, '71, and '73. Finally in California prices are dropping and should continue to drop for the next two years. In Cabernet Sauvignon look for the '74s, and in Chardonnay, '72, '73, or '74.

* * *

Next Month: More *Questions from Readers*—Let's have them!

Clinical Trials

By Oldden



CPAP Helps Weaning From Controlled Air In Respiration Failure

Medical Tribune Report

BOSTON—Results achieved in weaning patients from the controlled ventilation they required during acute respiratory failure indicate that persons at high risk for hypoxemia are best managed by a system that provides continuous positive airway pressure (CPAP) throughout all phases of spontaneous ventilation, according to Dr. Thomas W. Feeley, of Beth Israel Hospital.

Dr. Feeley defines two high-risk groups—patients who have been dependent on positive end-expiratory pressure while on controlled ventilation, and those with increased closing volume who usually develop airway collapse during tidal ventilation.

Patients weaned without CPAP undergo a "significant increase" in intrapulmonary right-to-left shunt whereas those with CPAP do not show the increase, Dr. Feeley said.

Patients weaned on CPAP also show significant improvement in vital capacity and maximum inspiratory force.

The following approach to management has yielded first-attempt success in about 80% of cases at Beth Israel:

- Patients are carefully evaluated for their readiness to have controlled ventilation discontinued by a number of tests—of pulmonary function, cardiovascular stability, metabolic rate, acid-base status.
- If findings are satisfactory, the patient is placed in a sitting position and the tracheal tube is connected to a T-piece or Briggs adaptor, which in turn is connected to a heated nebulizer. Inspired oxygen concentration is set approximately 10% higher than that required during controlled ventilation.
- Vital signs are monitored every five minutes at the start of the weaning process and a specimen of arterial blood is tested after the first 15 or 20 minutes.
- Controlled ventilation is resumed if the patient shows an unacceptable lowering of arterial oxygen tension or elevation of arterial carbon dioxide tension, or if clinical signs of hypoxemia or hypercapnia develop. Those who develop hypoxemia are weaned with CPAP.

IMMATERIA MEDICA

Medical Advice

That's the way the *Wall Street Journal* recently headed a brief item sent along by Dr. Edgar Richards of Long Island City. It read: "Consolidated Edison Co., at the request of the New York Heart Association, included a leaflet, "How to Tell You're Having a Heart Attack," with its . . . bills. Replied a Scarsdale, N.Y. doctor with his $158.76 payment: 'The juxtaposition of the booklet and your monthly bill is admirable. I would, however, suggest that if some way could be devised to have the customer read the booklet before the bill, many more lives could be saved.' "

Pages from the Past Today

We're indebted to the *Reporter*, a bulletin on academic affairs for the faculty and staff of the University of Michigan, for recounting how "a moment of levity," was introduced at the recent Congressional hearings on the National Science Foundation's budget for fiscal 1977. That moment came when, during his testimony, Thomas F. Jones, Vice-President for Research at Massachusetts Institute for Technology, recalled that there was a time when many people in universities and in Congress opposed research in the social sciences. He quoted the following colloquy of 30 years ago, which took place during Congressional hearings on the original National Science Foundation Act:

Committee member: "There is a sort of antipathy against social science that might make a difference in whether this legislation gets approval. I think we had better stick to fundamentals."

Witness (College president): "Your remarks, Congressman, are in effect a summary of the views of most of the scientists who have testified."

Committee member: "That is a very great compliment."

Witness: "We are just average fellows trying to do a job."

Committee member: "You are the experts."

Witness: "It seems to me essentially unsound to put into a National Science Foundation a wide range of social questions upon which the people of America have not yet made up their minds."

Committee member: "There would be a lot of short-haired women and long-haired men messing into everybody's personal lives."

Nobody we know, we trust.

From Sunny Florida—II

Our anonymous medical librarian in sunny Florida has noted "strange bedfellows" in the Audio-Digest family practice tape cassette: *Marriage Counseling; Minimal Brain Dysfunction.*"

The husband, no doubt, sez our librarian.

Self-Given Heparin Averts Embolisms In Risky Pregnancies

Medical Tribune World Service

DUBLIN—Self-administered injections of heparin have proven highly effective in averting thromboembolic complications in high-risk pregnant women, according to Dr. John Bonnar, of the Department of Obstetrics and Gynecology, Trinity College, here. Normally, such complications occur in two to five of every 1,000 deliveries, he told a joint meeting of the British, Canadian and Irish Medical Associations.

In his study, about 80 pregnant women self-injected heparin for periods of from two to 36 weeks in twice daily doses ranging from 10,000 to 25,000 units, Dr. Bonnar said. They continued to receive heparin throughout labor and delivery, as well as for six weeks following delivery. None of the women experienced thromboembolic complications throughout the entire heparin administration period, but ileofemoral thrombosis did occur in two patients when heparin use was stopped within 10 days of delivery.

Heparin is preferred to oral anticoagulants because the oral drugs are known to present serious hazards to the unborn infant. In some cases, the oral drugs have been linked to teratogenic effects including chondrodysplasia punctata, optic atrophy, cataract, mental retardation, and flexion contractures, Dr. Bonnar said adding that breast feeding is *not* contraindicated for the heparin takers.

Women admitted to the heparin program had experienced leg discomfort, swelling, slight cyanosis when standing, increased prominence of the superficial veins, and other conditions predisposing to thromboembolic complications. Also included were women to undergo Caesarean section, in which the clot problem frequently occurs.